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MICROCHEMICAL STUDIES OF ARSENIC IN ARSENICAL PIGMENTATION AND KERATOSES *

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For many years we have had accurate chemical methods for the detection of small amounts of arsenic in tissue. Studies have been made chemically and pathologically of every organ and tissue in the body following the various methods of arsenical administration. This paper will deal with a microchemical method for the study of arsenic in relation to the tissue cells. The existence of a satisfactory method offers a way to study the physiologic and pathologic effects of arsenic in several rather obscure conditions, such as arsenical keratoses, pigmentation and dermatitis, and the rôle played by arsenic in the production of epithelioma in psoriatic lesions.

In this paper will be given a detailed description of the method with controls and a study of arsenical keratoses and pigmentation. Justus,[1] in 1905, first employed this method and came to the conclusion that arsenic administered by mouth enters the blood stream in combination with the plasma of the erythrocytes. It enters all the organs, the cells of which take it up without distinction. He found arsenic in greatest amounts in the skin, kidneys, liver and intestines. He believed the arsenic was in the cytoplasm around the nucleus, but within the cell, and that the arsenic deposits were finer in the kidney and intestine and more coarse in muscle, liver, coil glands and epidermis. He evidently was unable to see, with the magnification available at that time, the actual individual crystals of the arsenic trisulphid and relied on the diffuse stippling given to the tissue by the arsenic deposits. As will be shown later, had he been able to see the individual crystals, his conclusions regarding the location of the arsenic in the cell would have been different.

* Read before the Section on Dermatology and Syphilology at the Seventy-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., May, 1925.

1. Justus, J.: Ueber Arsenvergiftung auf Grund einer mikrochemisch-histologischen Methode, Derm. Ztschr. **12**:277, 1905.

Again, in 1921, Brünauer [2] employed the same method with certain improvements in a study of arsenical keratoses. He concluded that the characteristics of arsenic trisulphid in tissue were: (1) It was a yellow brown color; (2) it consisted of fine, rounded and prolongated granules which never clumped together; and (3) the arsenic was practically all extracellular. He was unable to say definitely that any arsenic was intracellular. The location of the arsenic in the skin and its relation to the cells is of paramount importance in considering the pathology and physiology of the various conditions produced by arsenic.

THE METHOD

The method for the microchemical detection of arsenic in tissue used by the author was substantially the same as that used by Brünauer, with certain variations. The method was as follows:

1. The tissue was fixed in 10 per cent. dilution of solution of formaldehyd for from twenty-four to forty-eight hours.

2. It was then washed in running tap water for at least six hours.

3. The tissue was then cut in small pieces not more than 2 mm. thick.

4. The pieces of tissue were placed in a one ounce, ground glass, stoppered bottle, and the bottle was nearly filled with fresh, neutral hydrogen sulphid solution. A small amount of petrolatum was placed on the stopper, inserted tightly, and then bound down with a tape or cord. The bottle and contents were incubated at from 70 to 80 C. for four days. Since this procedure greatly reduces the staining power of the tissue, incubating at 56 C. for six days was tried, with satisfactory results, and considerable staining power was preserved. The neutral hydrogen sulphid was changed daily. This process caused the surface of the tissue to turn dirty gray to black, due to precipitated iron sulphid.

5. The tissue was next washed in running water for from six to twelve hours.

6. It was then dehydrated by successive passages through 50, 70, 80, 95 per cent. and absolute alcohol, each containing about 10 per cent. of ether.

7. The tissue was next imbedded in celloidin and cut in sections not over 5 microns in thickness.

8. The cut sections were placed for twenty minutes in 10 per cent. hydrochloric acid which had been diluted with alcohol. This procedure is essential, since all sulphids precipitated by hydrogen sulphid, except

2. Brünauer, S. R.: Ueber mikrochemisch-histologisch nachgewiesenes Arsen bei Hyperkeratosis arsenicalis, Arch. f. Dermat. u. Syph. **129**:186-198. 1921.

arsenic trisulphid, are soluble in 10 per cent. hydrochloric acid. It does, however, seriously impair the staining qualities of the tissue.

9. The sections were washed in 70 per cent. alcohol for twenty minutes and stained with hematoxylin and eosin.

10. Differentiation was carried out with 95 per cent. alcohol.

11. Sections were cleared in oil of cloves, and the excess was removed with xylol.

12. Sections were mounted in Canada balsam.

CHARACTERISTICS OF ARSENIC TRISULPHID

The arsenic trisulphid has the following characteristics:

1. The gross precipitate in a test tube has the familiar bright yellow color of orpiment.

2. On a microscopic slide, the individual crystals are seen to be nearly round or oval but somewhat irregular. Their diameter varies from 0.0005 to 0.00075 mm. Their color is yellow with a faint greenish tinge. When exactly in focus, the crystals appear solid with a bright halo. If too near the objective, they have a heavy rim, a clear center and a slight halo; whereas, if they are beyond the exact focus, they have a clear center, a rather faint rim and little or no halo.

3. In tissue, the crystals of arsenic trisulphid have about the same characteristics as on a slide. They have a greenish-yellow tinge and vary a little more in size. Brünauer could not say that any arsenic was present inside the cell in his study of arsenical keratoses. As shown in Figures 1 and 2, there can be little doubt that some arsenic does exist inside the cell. Figure 1 shows the center of a liver lobule, and Figure 2, a convoluted tubule of a kidney removed from a rabbit one hour after receiving 0.05 gm. of arsphenamin. With exactly the same magnification, the arsenic in the kidney is apparently in larger crystals than in the liver. One other point worthy of mention is that there is no clumping of the arsenic. Only occasionally will two crystals be seen side by side.

PROOF OF ARSENIC

The question naturally arises, How does one know that this is arsenic? The following checks have been carried out in order to prove as far as possible that the deposits were actually arsenic trisulphid:

1. Crystals of pure arsenic trisulphid have the same microscopic appearance as those seen in the tissue section.

2. Under the chemical conditions existing, arsenic, if present, must be precipitated as the trisulphid, as shown by Carlson.[3] It is true that

3. Carlson, C. E.: Eine neue Methode zum leichten Nachweis und zur raschen Ausscheidung von Arsen und gewissen Metallsalzen aus Flüssigkeiten, Ztschr. f. physiol. Chemie **68**:243, 1910.

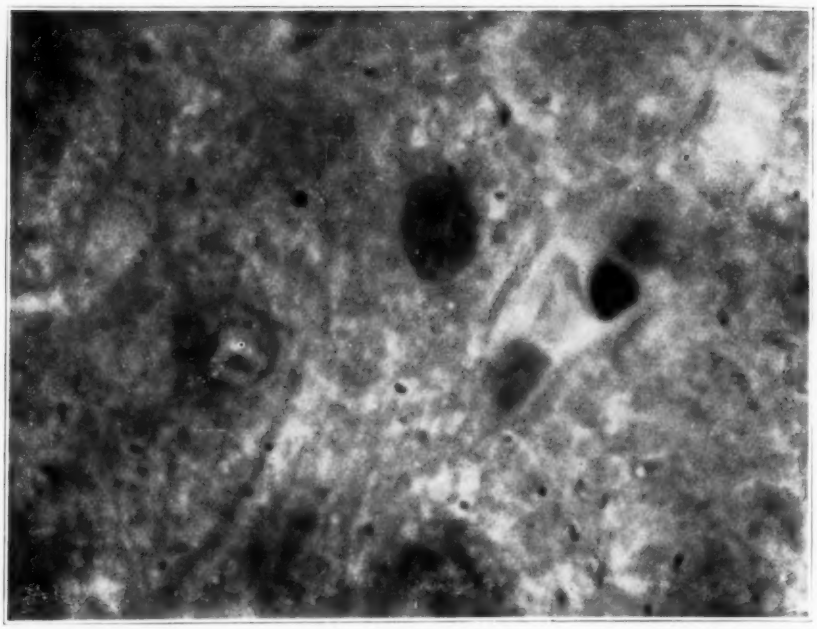

Fig. 1.—Prepared for arsenic. Rabbit liver from an animal receiving 0.05 gm. of arsphenamin one hour before death. Most of the arsenic is intercellular, but apparently some is inside the cell. Same tissue with usual staining methods showed no arsenic. Magnification, 1 × 3,880.

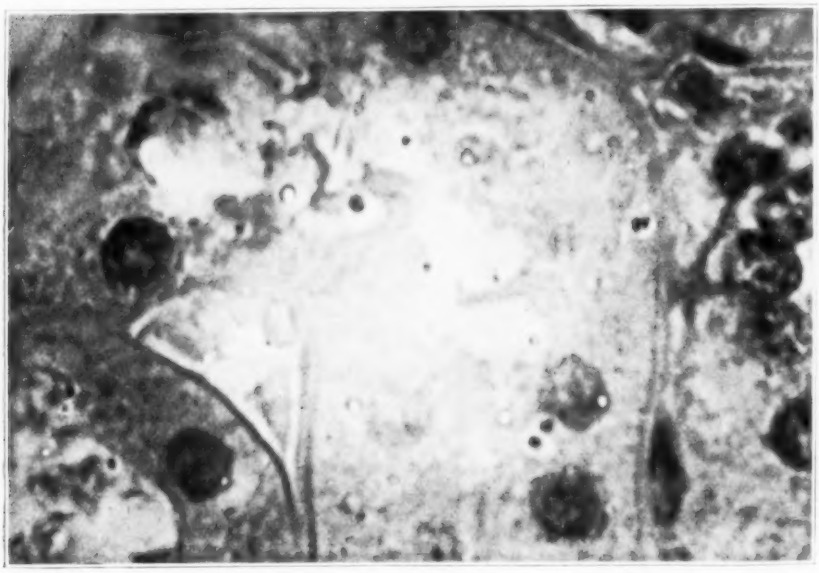

Fig. 2.—Prepared for arsenic. Rabbit kidney from an animal receiving 0.05 gm. of arsphenamin one hour before death. Some of the arsenic is apparently inside the cell. Magnification, 1 × 3,880.

arsenic trisulphid precipitates more readily in an acid solution, but it will also precipitate in a neutral solution if incubated long enough at 70 to 80 C. Arsenic trisulphid is precipitated from solutions of an arsenate as well as of an arsenite, since the hydrogen sulphid gradually reduces the arsenate to an arsenite.

3. The precipitate is not iron sulphid nor any of the other metallic sulphids, because they are soluble in 10 per cent. hydrochloric acid.

4. The precipitate is not sulphur, since sulphur is soluble in alcohol, ether, celloidin and xylol. Microscopically, sulphur has entirely different characteristics than arsenic trisulphid.

5. The crystals are not deposits of blood pigment, because they have entirely different microscopic appearances as to size, shape, clumping, refractility.

6. Sections of skin studied for arsenic were also stained for pigment. There is no difficulty in differentiating them, since pigment granules are not crystalline, are clumped together and intracellular.

7. Normal human and rabbit skins were examined for arsenic and found to be entirely negative.

8. Rabbits were given intravenous injections of arsphenamin, and their organs were found to contain typical deposits of arsenic when prepared by the foregoing method (Figs. 1 and 2). These same tissues when prepared by the usual paraffin imbedding and hematoxylin and eosin staining were found to be free from anything simulating the arsenic trisulphid seen in the sections prepared for arsenic.

9. Sulphids of iron, mercury, bismuth, arsenic and lead were prepared in separate test tubes and subjected to the same procedures as those carried out in the method for tissue. The arsenic trisulphid alone was present at the completion of the experiment.

10. Sections of tissue studied for arsenic were also prepared with potassium ferrocyanid and acid-alcohol for iron. No iron was demonstrable except when blood pigment was present.

ARSENICAL KERATOSES

Mr. B. presented himself for examination on October 6, 1924. He showed typical arsenical keratoses of the palms and soles unaccompanied by hyperhidrosis; in fact, the amount of perspiration present seemed to be about normal. Each keratosis was, however, surrounded by a narrow zone of hyperemia. The lesions appeared three years previously, following the taking of "drops" for three months. Since that time he had had many new lesions, while the older lesions gradually regressed. A section of tissue 1 cm. in diameter containing a new keratosis was removed for study. It was divided in half and fixed in 10 per cent. dilution of solution of formaldehyd. One piece was prepared in the usual manner with paraffin imbedding and stained with hematoxylin and eosin. The other piece was prepared by the method described above for arsenic.

Fig. 3.—Prepared for arsenic. The center of an arsenical keratosis is shown. Note the large split in the lower horny layer and the area of necrosis below it in the epidermis. This gives an idea of the degree of staining power retained by the tissue after preparation for arsenic. Magnification, 1 × 100.

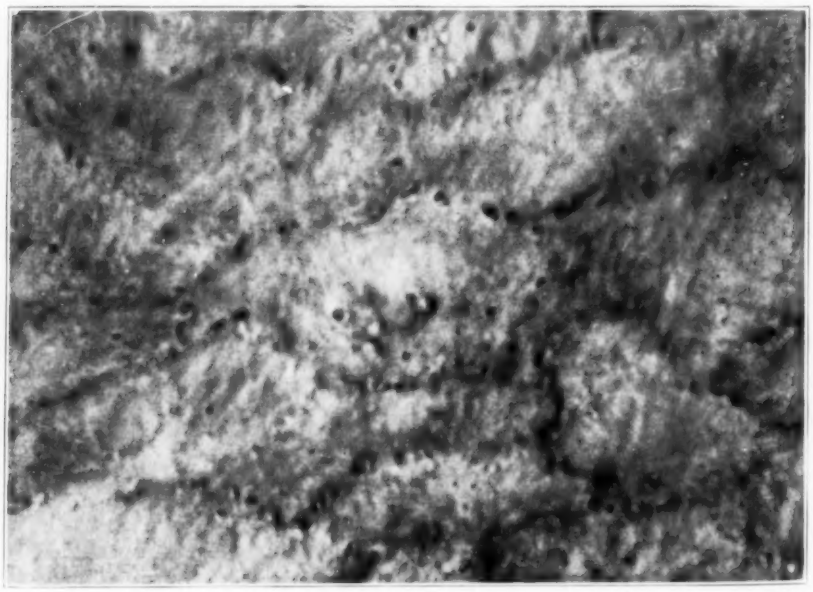

Fig. 4.—Prepared for arsenic. Horny layer in an arsenical keratosis. Arsenic is intercellular and evenly distributed throughout. Magnification, 1 × 3,880.

Histologically, the findings were typical of an arsenical keratosis and did not vary in any respect from those of previous observers. A short summary of the histology will be given in order to compare it with the findings in regard to the arsenic deposits (Fig. 3).

1. The horny layer was markedly hyperkeratotic and pierced only by sweat ducts which appeared compressed. In the center of the keratosis, the cells were split apart, leaving an open space. These splits varied in size and number in different sections (Fig. 3).

2. The stratum lucidum apparently was normal.

3. Stratum granulosum was marked. The upper two or three layers of cells were filled with keratohyalin granules. In the center of the keratosis were numerous areas of local cell death which were directly beneath the splits in the horny layer.

4. The stratum spinosum showed these same areas of necrosis, which extended down to and involved the basal layer.

5. The rete pegs were elongated and compressed.

6. In the papillae there was an increase in vascularity with perivascular infiltration.

7. The connective tissue showed chronic inflammatory changes generally distributed.

8. The coil glands and ducts showed little, if any, change, except where the ducts entered the epidermis. At that point there was considerable chronic inflammation. This fact is of major importance in considering the mode of development of the keratosis. Numerous observers have called attention to the hyperhidrosis associated with the arsenical keratoses and have thought that the keratoses began around the sweat ducts. Just as competent observers have recorded patients with normal perspiration, and in Stahl's[4] patient a pre-existing hyperhidrosis cleared up on the appearance of the keratoses. In one case, that of Heuss,[5] an anhidrosis was present. The author has observed numerous cases of arsenical keratoses with and without an associated hyperhidrosis.

ARSENIC FINDINGS

Photomicrographs of tissue prepared for arsenic showed the following in sections from an arsenical keratosis:

1. In the horny layer (Fig. 4), the arsenic trisulphid was evenly distributed between the cells. It was impossible to say, even with careful focusing, that any arsenic existed inside the cell. Not only was the arsenic present in the horny layer of the keratosis, but also to a lesser degree in the corneum of the normal skin surrounding the keratosis.

2. Stratum granulosum and stratum spinosum down to and including the basal layer contained a great deal of arsenic. The deposits were

4. Stahl, quoted by Brünauer: Arch. f. Dermat. u. Syph. **129**:186, 1921.

5. Heuss, E.: Zwei Fälle von Keratosis und Melanosis nach innerlichem Arsengebrauch, Cor.-Bl. f. schweiz. Aerzte 1894, No. 94, p. 301.

Fig. 5.—Prepared for arsenic. A papilla with adjacent basal layers of the epidermis in an arsenical keratosis. Some arsenic is apparently intracellular. Most of the arsenic is in this area. Magnification, 1 × 3,880.

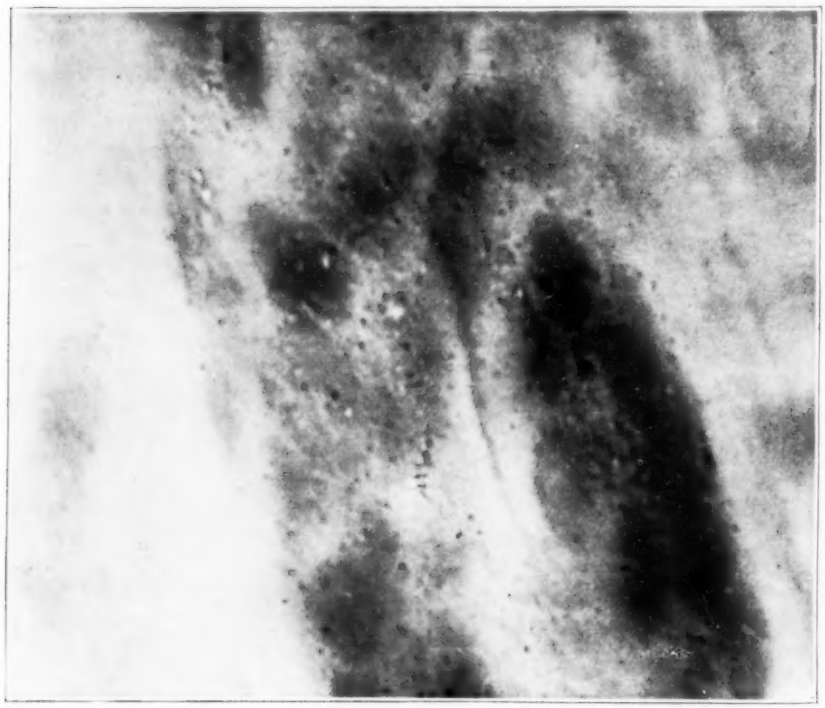

Fig. 6.—Prepared for arsenic. A coil duct in an arsenical keratosis just before entering the epidermis. There is about the same amount of arsenic present as in any papilla. No arsenic could be found in the coil gland. Magnification, 1 × 3,880.

particularly marked immediately surrounding the areas of necrosis. These same layers in the normal epidermis between the keratoses contained arsenic, but in smaller amounts. It was impossible to say positively that any arsenic was present inside the cell, but it is extremely probable that such was the case, as shown in Figure 5.

3. The area of greatest arsenic deposit was in the basal layers of the epidermis and in the papillae of the corium, especially under the areas of necrosis in the epidermis mentioned above (Fig. 5). Although most of the arsenic was in the intracellular spaces, some apparently existed inside the cell, but this could not be stated positively.

4. In the corium proper, a small amount of arsenic was seen in the intercellular spaces. The coil gland ducts nearing the epidermis contained about as much arsenic as did the papillae and epidermis, but none was present in the coil glands themselves. The arsenic was evenly distributed throughout the wall of the ducts just as in the epithelium, and very little arsenic was seen in the lumen (Fig. 6).

COMMENT

In Brünauer's case, in which there was an associated hyperhidrosis, he found large quantities of arsenic in the coil glands and ducts, in addition to the papillae and epidermis. The foregoing findings are definite proof that the coil glands need not necessarily be the dominant factor, as Brünauer supposed, in the production of arsenical keratoses. The bulk of the arsenic is apparently deposited in the areas of greatest vascularity and gradually passed outward intracellulary. Since this study was completed, tissue from another patient with arsenical keratoses with associated hyperhidrosis, was secured. In addition to the findings stated above, arsenic in small quantities was found in the coil glands. The mechanism of the production of arsenical keratoses would seem to be the speeding up of the keratinization cycle by the deposit of an irritant, in the form of arsenic, in the upper corium, papillae and epidermis. The coil glands need not necessarily be involved in the process.

It was hoped that this study might contribute something to the etiology of epithelioma developing in an arsenical keratosis. In this connection, it is well to recall the excellent work of Binz and Schulz,[6] back in 1879, and concurred in by Brooke and Roberts,[7] and Wile,[8] that

6. Binz, C., and Schultz, H.: Die Arsengiftwirkungen vom chemischen Standpunkt betrachtet, Arch. f. exper. Path. u. Pharmakol. **11**:200, 1879.

7. Brooke, H. G., and Roberts, L.: The Action of Arsenic on the Skin as Observed in the Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Dermat. **13**:121, 1901.

8. Wile, Udo J.: Arsenical Cancer with Report of a Case, J. Cutan. Dis. **30**:192, 1912.

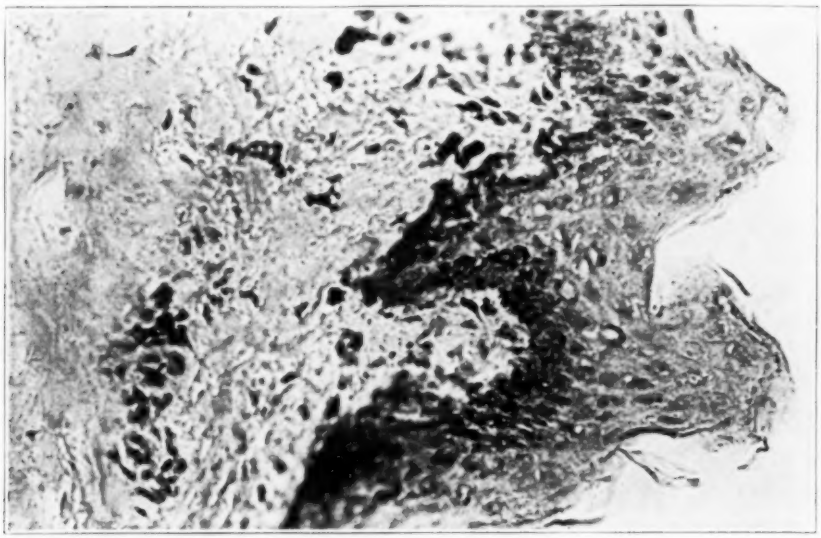

Fig. 7.—Paraffin imbedding, polychrome-methylene blue stain. Shows the location of the pigment in arsenical pigmentation. The large mass of the pigment is around the arterioles in the papillae and upper corium. Note also the pigment in the upper layers of the epidermis. Magnification, 1 × 840.

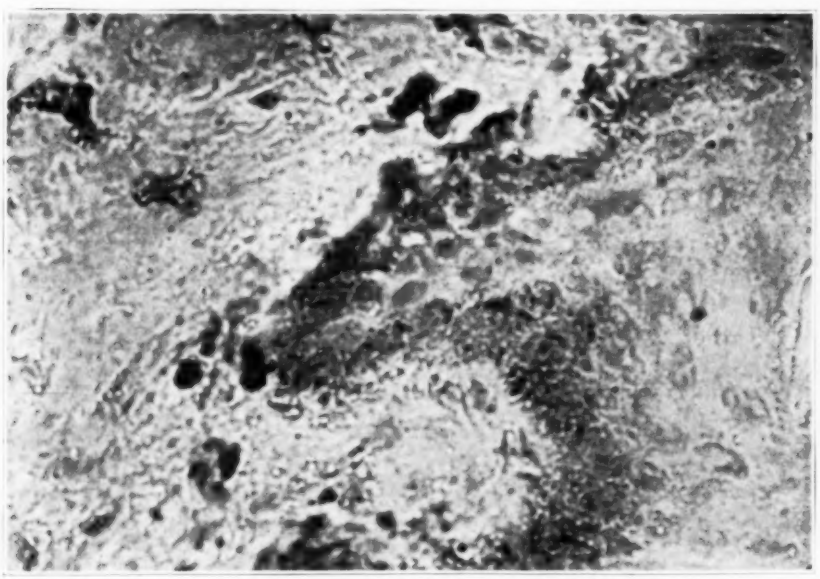

Fig. 8.—Paraffin imbedding, polychrome-methylene blue stain. Shows the location of the pigment in arsenical pigmentation to be in the corium. Magnification, 1 × 840.

the action of arsenic in living tissue is one of oxidation and reduction. Because of the increased supply of oxygen, the activities of the cells are greatly increased and carried on to the point of exhaustion and death. It is my belief that because of this chemical stimulation, the cells of the epidermis may undergo malignant changes.

ARSENICAL PIGMENTATION

A section of skin 2 cm. long and 1 cm. wide was secured from the back of a patient with typical arsenical pigmentation of the skin. He had also a peripheral neuritis in both upper and lower extremities and a wrist and foot drop. For six weeks previously he had received weekly intravenous injections of an arsenical preparation, the composition of which was unknown. The tissue was prepared in the same manner as in the case of arsenical keratoses. Special stains were used for iron and pigment.

A summary of the pathologic findings will be given in order to compare them with the findings in regard to the arsenic. They agree with those of Gans,[9] Brooke and Roberts, and Wyss,[10] with certain minor variations.

1. The epidermis was generally thickened, owing to increase in stratum spinosum, stratum granulosum, and particularly the horny layer, which in some areas was exfoliating. The rete pegs were prolonged in many instances, owing to edema and inflammatory changes in the papillae.

2. In the upper part of the cutis, there was marked perivascular infiltration of round cells and mast cells extending up into the papillae. There was an increase and dilatation of the small arterioles and lymph spaces, with a great deal of edema of the entire upper part of the corium. Orcein staining showed marked destruction of the elastin and collagen which Gans believed characteristic of arsenical pigmentation.

3. The pigment was chiefly in the papillae and upper half of the corium located around the arterioles and capillaries in cells arising from them (Fig. 7). These areas were also the areas of infiltration. Some of the mast cells contained a few pigment granules. No pigment was seen extracellularly. In the epidermis there was a definite increase in pigment in the basal layer, and here and there in the stratum spinosum and stratum granulosum. This pigment was granular and intracellular in the cytoplasm around the nucleus. By far the bulk of the pigment was in the corium.

9. Gans, Oscar: Zur Histologie der Arsenmelanose, Beitr. z. path. Anat. u. allgem. Pathol. **60**:22, 1915.

10. Wyss, O.: Ueber Arsenmelanose, Cor.-Bl. f. schweiz. Aerzte, 1890, No. 15, p. 473.

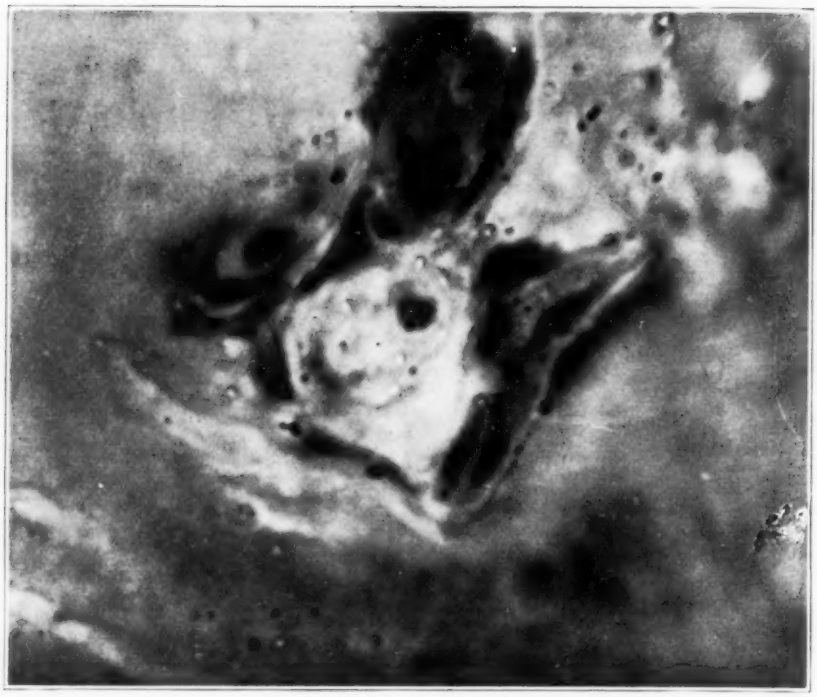

Fig. 9.—Prepared for arsenic. A small arteriole in the corium of a case of arsenical pigmentation, showing the arsenic in relation to the pigment-containing cells apparently arising from the wall of the arteriole. Magnification, 1 × 3,880.

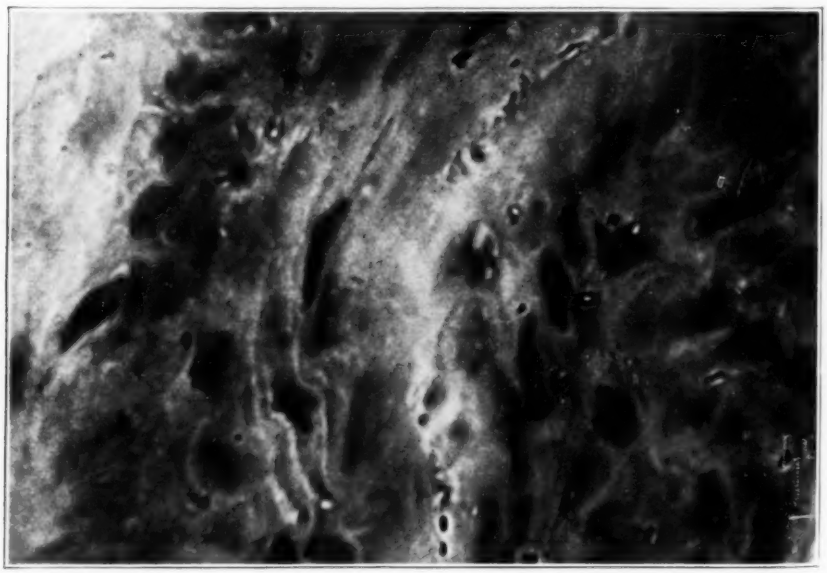

Fig. 10.—Prepared for arsenic. A coil gland duct just entering the epidermis and showing arsenic in the lumen of the duct, wall of the duct and epidermis. Magnification, 1 × 3,880.

ARSENIC FINDINGS

Examination of sections prepared for arsenic showed the following:

1. The entire epidermis contained a great deal of arsenic. In the lower layers, some of it was apparently inside the cells, although, as in the case of arsenical keratoses, this could not be positively stated. It was distributed evenly and in no relation to the amount of pigment (Fig. 8).

2. The upper half of the corium contained surprisingly large amounts of arsenic, particularly in the papillae and in the intercellular spaces surrounding the arterioles (Fig. 9). The arsenic, however, was in large amounts in every part of the upper corium, whether pigment was present or not, and was separate and distinct from the pigment.

3. The coil glands and ducts contained a small amount of arsenic (Fig. 10).

4. The sebaceous glands and ducts contained large quantities of arsenic (Fig. 11).

5. Considerable arsenic was found in the hair follicles, including all the layers of the sheath and the hair itself (Fig. 12).

COMMENT

It is not the purpose of the author nor within the scope of this paper to discuss all the theories advanced as to the origin and nature of pigment. I do believe, however, that the facts presented may throw some light on the origin of pigment. In the first place, we know definitely that through some action of arsenic a melanosis is produced. Heuss thought that the pigment itself contained the arsenic. The present study effectually disproves that. Through the work of Gans [9] and Kreibich,[11] we know that the pigment contains lipoids and melanin and does not arise from the products of broken-down blood. It must be due, then, to cell metabolism and the formation of new products with those at hand. Bloch [12] thought that the oxidizing ferment, called by him "dopa oxydase," in the epidermal cells acted on dioxyphenylalanin to produce pigment, dioxyphenylalanin, or "dopa," being the mother substance of normal pigment. This reaction took place only in the epidermis. Kreibich obtained the same results as Bloch, but found that para-di-methylphenylendiamin gave the same reaction as "dopa."

11. Kreibich, C.: Zu Blochs Dopareaktion, Dermat. Wchnschr. **66**:193, 1918.

12. Bloch and Ryhiner: Histochemische Studien an überlebenden Geweben über fermentative Oxydation und Pigmentbildung, Ztschr. f. d. ges. exper. Med., **5**:179, 1917; Chemische Untersuchungen über das spezifische pigmentbildende Ferment der Haut (die Dopaoxydase), Ztschr. f. physiol. Chemie **98**:226, 1917; Das Problem der Pigmentbildung in der Haut., Arch. f. Dermat. u. Syph. **24**:129, 1917.

Fig. 11.—Prepared for arsenic. A sebaceous gland in a case of arsenical pigmentation. Note the large amount of arsenic present. The sebaceous ducts also contain a great deal of arsenic. Magnification, 1 × 3,880.

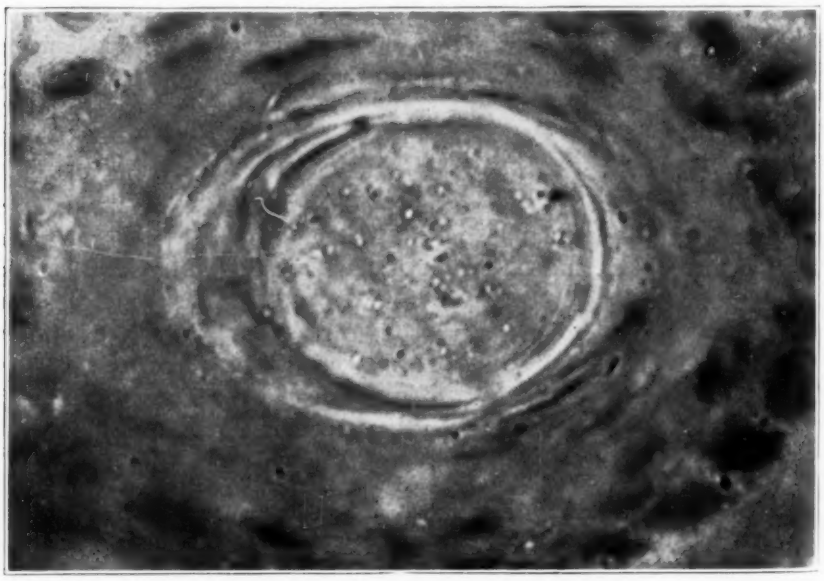

Fig. 12.—Prepared for arsenic. A cross section of a hair shaft and its follicle deep in the corium in a case of arsenical pigmentation. Arsenic is seen in the hair shaft and around it, and in the follicle. Magnification, 1 × 3,880.

Meirowsky [13] agreed with Bloch in the main points, but could not follow him in the point that all pigment was formed in the epidermis. From my own work and that of Gans and others, I must conclude that the melanotic pigment seen in arsenical pigmentation does arise in the corium principally and probably also to a much less extent in the epidermis. If the theory of Bloch that melanin is formed from promelanin by an oxidative enzyme is true, then it is reasonable to suppose that the arsenic acts either directly as an oxidizing agent on the promelanin to form melanin or else indirectly by setting up an inflammatory reaction with perivascular infiltration, liberating the oxydase in that manner. If the action of the arsenic is direct, one would expect pigment production in other tissues in the body, unless the promelanin exists only in the skin, which is extremely unlikely. It is, therefore, the author's theory that arsenic acts indirectly on the mother substance of melanin to form the finished product.

SUMMARY

1. There exists a satisfactory method for the microchemical study of arsenic in tissue, which has been employed by the author in the study of arsenical keratoses and pigmentation. A detailed description of the method with controls is given.

2. A detailed study of arsenical keratoses is given with photomicrographs showing the location of the arsenic deposits. The mechanism of the production of arsenical keratoses is discussed and its bearing on the development of epitheliomas.

3. A detailed study of arsenical pigmentation is given with photomicrographs showing the relation of the arsenic to all the cutaneous structures. A discussion of the probable action of arsenic in the production of pigment is given.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich: I believe that Dr. Osborne has presented a piece of scientific investigation of real value. Any one who has done any chemical work with arsenic will realize how difficult it is to be perfectly sure that one's chemical formula and so-called normal constituents are free from the drug, and it speaks for the thoroughness with which Dr. Osborne has prepared this paper that he has controlled his experiments with normal skin to be sure that there was nothing in the nature of artefacts.

I am sorry that Dr. Osborne could not go on with his paper and draw his conclusions. He has shown that the arsenical pigmentation is entirely different from that of the heavy metals, notably silver, in which case the pigment is due to the deposit of the heavy metal itself.

13. Meirowsky, E.: Ueber den Ursprung des melanotischen Pigments der Haut und des Auges, Leipzig, 1908; Das Problem der Pigmentbildung im Lichte der neuen Forschungen Blochs und seiner Mitarbeiter, Dermat. Ztschr. **24**:705, 1917.

There were one or two things which were not clear to me which I hope he will explain in his discussion. Arsenic would appear to produce on the one hand the pigment and on the other hand the keratosis. It would be interesting to hear from him why in the case of the keratoses themselves when so large a deposit of arsenic is found one does not find the pigment in the sections. The relation of the keratosis to epithelioma is a point which Dr. Osborne stressed in his paper but which was not brought out owing to the lack of time.

Dr. Earl D. Osborne, Buffalo: I feel from examining the sections of arsenical keratosis that the logical explanation for the development of epithelioma is that the bulk of the arsenic is deposited in the papillary and subpapillary layers of the skin. It has been shown by Binz and Schulz that the action of arsenic in the body is one of oxidation and stimulation of cells. If that is the case, stimulation of the basal layer might well offer the explanation for the formation of epithelioma.

As Dr. Wile said, I did not have time to take up the question of pigmentation in arsenical pigmentation. It is my belief, briefly, that arsenic acts in an indirect way in the formation of pigment. It cannot act directly, else we would have pigment in all the organs of the body, so it must have an indirect action in the corium at the point at which the precursors of pigment come in contact with the arsenic.

In regard to the medicolegal aspect, there is no reason why this method should not be of great value, exactly as Dr. Smith mentioned. I have had the opportunity of studying one case in which the patient died from arsenical exfoliative dermatitis, and there was no difficulty in demonstrating the arsenic in the various organs and tissues.

THRUSH INFECTIONS OF THE SKIN*

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Among the innumerable fungus diseases of the skin, thrush infection is one of the most recent, the knowledge that this organism is capable of exciting cutaneous eruptions being in reality an acquisition of the past ten years. The causative agent in these eruptions, *Oidium albicans*, or thrush fungus, belongs to those first micro-organisms which were studied with the help of the microscope about eighty years ago; yet thrush infections of the mucous membranes, and especially oral thrush infection, have long been known. Until recent years, however, we have been prone to consider thrush infections as limited to the mouths of nursing infants or to the vagina of pregnant women—less frequently with localization on other mucous membranes, as in the nose, larynx, esophagus, bladder and urethra. These various lesions of the mucous membrane have, for the most part, been of benign character; yet, at times, this apparently harmless fungus has broken through the mucous membrane, gained entrance into the blood vessels and thereby excited a general systemic, and not infrequently, lethal infection.

During recent years a great many skin eruptions formerly considered as "eczema" and like affections have been found to owe their etiology to this fungus. The cause for this rather late conviction that the thrush fungus is capable of exciting skin eruptions is due, on one hand, to the fact that the pathogenicity of this fungus is really a minimal one; and, on the other hand, to the fact that this fungus is occasionally found as an inhabitant of normal skin, its cultural demonstration from skin lesions thereby having a limited significance. From the many accurately studied cases thus far reported in the literature, there can now be no doubt that this fungus does, under favorable conditions, excite lesions of the skin. These occur as disseminated lesions over large areas of the skin surface (thrush infections seen in water-bed treatment, after wet dressings, in nursing infants, etc.) or are found localized in the form of isolated lesions in the contact areas of the skin (anus, genitals, under the breasts, in axillary and interdigital folds, etc.) where the warmth and moisture are especially favorable for the growth of the fungus. New localizations are rapidly being added to this list.

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THRUSH INFECTIONS OF THE CONTINUOUS BATH

This type of thrush infection was first described by Jacobi [1] in 1907, Kuster [2] a few months later reporting the bacterial findings in these cases. Kraepelin,[3] in 1901, had seen types of this infection, yet this observer was apparently unaware of the fungous nature of the eruption. In 1921, a number of these cases were reported by Kumer [4] from the water-bed station of the Riehl clinic.

According to Jacobi, the water-bed mycosis is a constant accompaniment of this type of therapy; yet at the Riehl clinic only sporadic cases were seen outside of a rather short-lived epidemic. Jacobi observed as primary efflorescence in these cases dark red, slightly infiltrated papules, which, through peripheral growth and confluence with similar contiguous lesions, formed larger areas with polycylic borders. These larger plaques were characterized by a livid red central area surrounded by an elevated border of whitish epithelial accumulation, the entire lesion in turn being surrounded by a bright red areola. In Kumer's cases both bright red papules and pinhead vesicles occurred as primary efflorescences.

At times these papules and vesicles are so thickly studded over the affected area that the part seems diffusely involved. The sites of predilection of the affection are those areas of the skin surface which are alternately exposed to water and air, as the axillae, knees and hands. The genital and anal regions are often markedly involved, and at times the greater part of the body may be affected. The eruption is, as a rule, most pronounced on the palms, in the region of the nails and in the interdigital folds; in the latter location, typical interdigital erosions (so-called erosio interdigitalis blastomycitica of Fabry) are seen.

I have recently had the opportunity of studying one case of this type of thrush infection in a patient at the water-bed station of the Riehl clinic. The eruption in this case was identical with those described by Kumer. In addition to thickly studded vesicles, pinhead to pea-sized scaling papules and small coin-sized plaques of erythema and scaling on the knees and in the axilla, the hands showed typical

1. Jacobi: Eine besondere Form der Trichophytie als Folgeerscheinungen des permanenten Bades, Arch. f. Dermat. u. Syph. **84**:289, 1907.

2. Kuster: Untersuchungen über ein bei Anwendung von Sauerbadern beobachtes Ekzem, München. med. Wchnschr. **32**:1571, 1907; Ueber die Ursache der Hauterkrankung bei Anwendung von Dauerbadern, Arch. f. Hyg. **62**:365, 1907.

3. Kraepelin: Zentralbl. f. Nervenheilk u. Psychiat. 1901, p. 711.

4. Kumer: Ueber die Wasserbettmycose, Arch. f. Dermat. u. Syph. **136**:12, 1921; Ueber eine Form der Chronischen Paronychie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **33**:160, 1921; Die Soormykose der Haut, Arch. f. Dermat. u. Syph. **140**:137, 1922.

but rather pronounced involvement. The palms and the palmar surfaces and webs of the fingers of both hands were covered with pinhead to pea-sized, thickly set vesicles, the case resembling the eruption occasionally seen in the so-called dyshidrosis, except that the vesicle roofs were more sodden than observed in the latter condition. After three or four days the vesicles ruptured, leaving the bright red vesicle floor exposed. At this period the palms appeared studded with pinhead to

Fig. 1.—Thrush infection of the continuous bath.

pea-sized areas of erosion bordered by a narrow rim of sodden epidermis. By confluence of smaller lesions, larger areas with polycyclic borders were formed. The vesicles located on the webs of the fingers underwent similar changes, forming areas of typical interdigital erosion. Innumerable vesicles appeared on the skin surrounding the finger nails, and on one finger, lesions formed between the nail and its matrix, the nail being elevated from its bed and the intervening space filled with a mass of sodden epidermis.

The microscopic examination of scales and particles of epidermis of the vesicle roofs revealed a fungus identical with that reported by Kuster and Kumer—veritable masses of long, thin, straight and branching mycelial threads and spores arranged in clusters or scattered along the mycelial threads. Septate filaments with side and terminal budding were occasionally encountered. On culture the large spore, gelatin liquefying variety of *Oidium albicans* was grown, frequently in pure culture.

THRUSH ERUPTION IN NURSING INFANTS

This second type of thrush infection was first described by Beck [5] in Budapest (1910) and independently by Ibrahim in Munich a few months later. Beck,[6] in 1915, gave a more detailed report of these cases. In the same year Schamberg [7] in America presented an extensive fatal case before the Philadelphia Pediatric Society, and Kaufmann-Wolf [8] in Berlin reported a similar case. In reality, this condition seems to have been described much earlier by Jaquet [9] under the title "Dermite erythemato-squameuse," although this observer was apparently unaware of the fungous nature of the eruption.

This eruption is not an infrequent one and is seen in normal infants as well as in infants suffering from thrush infection of the mouth or intestinal derangement. The primary efflorescences are superficially situated, pinhead vesicles which frequently become pustular, or lentil-sized areas of erythema with branlike scaling in the central portions. The vesicles and pustules soon rupture, leaving behind small denuded areas surrounded by a collar of undermined epidermis. These areas, as well as the initial small areas of erythema, extend peripherally to form small coin sized erythematosquamous patches with elevated borders. Through confluence of smaller lesions larger patches are formed, these not infrequently covering large areas on the body surface.

Near these larger patches isolated vesicles and smaller areas of erythema and scaling are usually found. The individual lesions are occasionally larger and show a greater tendency to crusting and scaling

5. Beck: Ueber das Erythema mycoticum infantile, Dermat. Studien **20**:494, 1910.

6. Beck: Neuere Beiträge zur Kenntnis des Erythema mycoticum infantile, Dermat. Wchnschr. **60**:301, 1915.

7. Schamberg: Memorandum on Cutaneous Thrush, Arch. Pediat. **32**:617, 1915.

8. Kaufmann-Wolf: Pilzerkrankungen der Hände, June Meeting, Berlin Dermat. Soc., Ref. Dermat. Ztschr. **21**:932, 1914; Zur Klassifizierung einiger Dermatomykosen, Dermat. Ztschr. **22**:441, 1915.

9. Jaquet: La pratique dermatologie, Paris, Masson et Cie, 1900.

(Schamberg,[10] Lombardo [11]) or resemble the lesions of herpes tonsurans (Kaufmann-Wolf's [8] case). The site of predilection of this eruption is the circumanal region, the disease not infrequently appearing to be from direct extension from the anal opening. From the region of the anus the lesions extend to the thighs, genitals, abdomen and buttocks. The skin of the trunk, neck and extremities are not infrequently the site of the eruption, and Schamberg's patient presented lesions on the scalp and face. In Kaufmann-Wolf's case a typical interdigital erosion was present on the hands. Dubreuilh and Joulia [12] have reported an almost generalized intertrigo of thrush origin in an infant, and Rasch [13] has more recently reported a somewhat similar case. In cases reported by Schamberg and Kumer, the skin of the breasts of the nursing mother was also infected from lesions in the mouth of the infant.

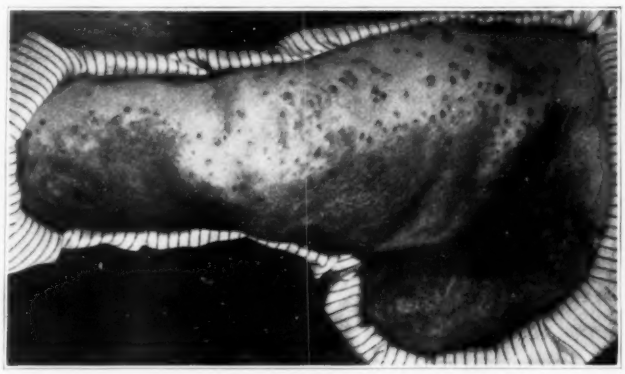

Fig. 2.—Thrush eruption in a nursing infant.

In these various cases *Oidium albicans*, or a closely related fungus, was demonstrated microscopically and culturally in the various skin and oral lesions. A case corresponding to those reported by Beck and Ibrahim will be briefly mentioned here.

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10. Schamberg: Memorandum on Cutaneous Thrush, Arch. Pediat. **32**:617, 1915.

11. Lombardo: Dermite endomicetica interdigitale, Gior. ital. d. mal. ven. **57**:594, 1922; XII Reunion of the Italian Society of Dermatology, Ref. ann. de dermat. et syph. **45**:137, 1923; Nuove osservazions di endomicosi cutanea, Gior. ital. d. mal. ven. **64**:563, 1923; Les Epidermomycoses. 1. Congress French Dermat. & Syph., Paris, June, 1922; Presse méd. **30**:559, 1922.

12. Dubreuilh and Joulia: De l'intertrigo mycosique-forme nouvelle d'epidermophytie due a une levure, Bull. Soc. franç. de dermat. et syph. **28**:192, 1921; Ann. de dermat. et syph. **3**:145, 1922; La question des Intertrigo mycoses, Ann. de dermat. et syph., February, 1924.

13. Rasch: Eczema marginatum Hebra and other Mycoses Resembling Eczema, Acta dermat. ven. **111**:315 (Dec.) 1922.

C. H., aged 5 weeks, presented a widespread thrush infection of the oral mucous membrane and an erythematosquamous and vesicular eruption over the body. In the anal region, about the genitals, and on the inner surface of the thighs and legs the skin was erythematous, covered with fine scales, and here and there showed isolated vesicles and areas of weeping. In the surrounding area many vesicles the size of a pinhead and small areas of erythema and scaling were found. Over the lateral surface of the right leg, on the abdomen, arms and neck, there were similar areas varying in size from that of a coin to that of a palm, with polycyclic borders of heaped up epithelium and outlying vesicles and erythematous areas. On the soles and dorsal surfaces of the feet there were many isolated vesicles with a surrounding halo of erythema. Microscopic examination of scales, roofs of the vesicles and bits of the membrane of the mouth revealed innumerable mycelial threads and spores in the typical mulberry-like arrangement. Culturally, the fungus was found to be *Oidium albicans*. The vesicle contents showed either no organisms or an occasional sporelike body.

THRUSH INFECTIONS AFTER WET DRESSINGS AND OTHER FACTORS FAVORABLE FOR THE GROWTH OF THE FUNGUS

A further form of this type of mycotic infection is seen following wet dressings and similar conditions favorable for the development of the fungus. These eruptions show no typical localization, are found either on normal skin or superimposed on an already existing dermatosis, and are characterized by the presence of vesicles and pustules, often in herpetic arrangement. Through the confluence of single lesions large areas of the skin may become diffusely involved, the eruption then simulating the thrush infection seen in nursing infants. These vesicles and pustules are usually sharply limited to the area covered by the compresses so that the mere localization lends the suspicion that the eruption was caused by this therapy. In other cases the lesions spread far beyond the treated area, often affecting distant areas of the skin. The clinical diagnosis is not always easy to make; yet in doubtful cases one glance through the microscope usually suffices to settle the question. The roofs of the vesicular and pustular lesions show innumerable mycelia and spores in the characteristic mulberry arrangement.

Staheli [14] has reported a case in which a vesicular and pustular dermatitis developed in the vicinity of an indolent ulcer treated with wet dressings. The eruption spread to involve the leg diffusely and finally extended to involve the other leg, this member becoming studded with minute vesicles and pustules. In a similar case a vesicular and

14. Staheli: Drei Fälle von Hautentzundung verursacht durch Oidien (Dermatitis pustulosa oidiomycetica), Arch. f. Dermat. u. Syph. **134**:407, 1921.

pustular dermatitis appeared over the scrotum and thighs. In both cases microscopic examination of the vesicle contents showed no organisms, yet the roofs of these lesions showed numerous double contoured segmented mycelial threads and ovoid or round sporelike bodies. Particles of epidermis and the vesicle contents gave a pure culture of *Oidium albicans*. By inoculation of culture material from both cases onto normal skin and the inoculated area covered with a wet dressing for twenty-four hours, a similar dermatitis was caused. *Oidium albicans* was demonstrated microscopically and culturally in the lesions of this provoked eruption.

Kumer has reported three cases of thrush dermatitis following the application of liquor Burowii wet dressings. As in Staheli's cases, the primary efflorescence was a pinhead vesicle which frequently became pustular. In one of his reported cases, the patient had in addition a concomitant typical interdigital erosion of the fourth interdigital space of the right hand. *Oidium albicans* of thrush was demonstrated microscopically and culturally in the pustular and vesicular lesions and in particles of epidermis from the interdigital erosion. Staheli [14] describes one case of vesicular and pustular eruption independent of treatment with wet dressings. This case had previously been demonstrated by Miescher at the fourth congress of the Swiss Dermatological Society. In a patient with scleroderma of the right foot of many year's duration, a pustular dermatitis developed over the sclerodermic area, finally spreading to involve the entire right leg, which became reddened, edematous and studded with pinhead to pea-sized pustules. The microscopic examination of the contents of the pustule revealed no organisms, but the roofs of these pustular lesions showed mycelial threads and clusters of spores. Culturally, the fungus was found to be *Oidium albicans*. By inoculation of culture material onto the arm of another patient, this observer was able to reproduce a pustular dermatitis with cultural and microscopic findings as in the original case.

Miescher [15] has observed a widespread vesicular and pustular thrush eruption on the trunk and extremities of a hospital patient whose skin was slightly macerated from prolonged and continuous sweating. By inoculation of culture material into the right arms of two patients treated for a period of twenty-four hours with wet dressings of saline solution, a pustular dermatitis corresponding to the inoculated area was reproduced. A pure culture of *Oidium albicans* was obtained from these lesions. The left arms of these patients, used as control, showed no eruption from the wet dressings alone. In a case of thrush infec-

15. Miescher: Meeting Swiss Dermatological Society, August, 1912; Ref. Dermat. Zentralbl. **1**:60, 1921; Miliaria rubra oidiomycetica, Dermat. Wchnschr. **73**:1265, 1921.

tion of the genito-anal region, breasts and feet, Alexander also found pustules scattered over the body. *Oidium albicans* was demonstrated microscopically and culturally in the various lesions. This observer was able to produce a pustular dermatitis by the inoculation of normal skin with pure cultures of the thrush fungus obtained from skin lesions of this patient and from mouth lesions of infants and vaginal thrush infections of adults.

Lombardo has reported the case of a 7 year old boy with erythematosquamous, vesicular and pustular lesions over the body, a chronic thrush infection of the oral cavity, onychia of the right thumb with a surrounding area of erosion, bronchitis and enteritis. The lesions of the skin were for the most part miliary vesicles and pustules with follicular localization. The thrush fungus was demonstrated in the roofs of the vesicles and pustules, in the scales from other lesions, in particles of the affected nail and in membrane from the lesions of the mouth. The same fungus was cultivated from the various lesions of the skin, nail particles, bits of membrane from the oral lesions, sputum and feces. The author considered the eruption as the same type as that reported by Staheli and Miescher.

INTERTRIGINOUS THRUSH INFECTION

Intertriginous thrush infections of the inguinal and anal region were first reported by Muijs [16] in 1916, and later by Dubreuilh and Joulia in 1921. Hudelo and Montlaur [17] had previously presented two patients with this type of mycotic infection before the French Dermatological Society (June, 1914). Similar cases have also been reported by Bloch,[18] Engman,[19] Staheli,[14] Kumer,[4] Alexander Roach, Lange,[20] and others, and it seems probable that cases described by Weidman [21] belonged to this group. This last observer reports three cases of "what would ordinarily pass for tinea cruris." One patient also had lesions on the fingers and toes, and a second patient presented concomitant lesions in the anal region. "Scrapings from each case showed mycelial threads more slender than those seen in epidermophyton infection but the striking thing was the grouping of the spores into clusters."

16. Muijs: Endomyces Albicans als Ursache einer Epidermomycosis inguinalis Dermat. Wchnschr. **66**:65, 1922.

17. Hudelo and Montlaur: Epidermomycose eczematoide par parasites du genre des levures, Bull. Soc. franç. de dermat. et syph. **25**:403, 1914.

18. Bloch: Cor.-Bl. f. schweiz. Aerzte **46**:273, 1916.

19. Engman: A Peculiar Fungus Infection of the Skin (Soorpilze), Arch. Dermat. & Syph. **1**:370 (April) 1920.

20. Lange: Beitr. z. Klin. der Soormykose der Haut, Dermat. Wchnschr. **76**:429, 1923.

21. Weidman: Resemblance of Yeasts in Cutaneous Scrapings to Hyphomycetes, Arch. f. Dermat. & Syph. **5**:325, 1922.

Pictures and description of the fungus on culture also corresponded closely to those of the thrush fungus. I do not believe that ordinary yeasts are capable of producing mycelia in lesions of the skin. In my opinion, yeasts in filament form are found only in old cultures.

In these cases, as in other types of thrush infection, the primary efflorescences are pea-sized areas of slightly scaling erythema, vesicles and pustules, which again, by peripheral extension and confluence of neighboring lesions, form larger plaques with gyrate configuration of the borders. These borders are sharply differentiated from the normal skin and usually composed of a heaped-up mass of whitish epithelial accumulation. In contrast to this type, which resembles closely the thrush infection seen in nursing infants (Beck[6] and Ibrahim[22] types), a second form closely resembling the interdigital thrush infection is not infrequently seen. In this type a thick membrane-like, white and sodden epidermic sheet covers a bright red and often slightly weeping base. This type of lesion is most frequently encountered in the inguinal and gluteal folds. Although these two types of lesions are usually sharply differentiated from the normal skin, many primary efflorescences of scaling erythema and vesicles are always found in the vicinity of these larger plaques. The gluteal and anal folds are the sites of predilection of this type of infection; yet the scrotum, penis, vulva and inner portions of the thighs are not infrequently involved. The cases reported by Muijs were mostly those of hospital patients who became infected in the wards. This same author observed a thrush infection on the genitals of a married couple, the husband apparently having been infected from a vaginal thrush infection of the wife.

A like case of conjugal infection was observed by Dubreuilh and Joulia. Cases of diabetes with thrush infection of the genitocrural region have been reported by Bloch, Dubreuilh, Joulia and Alexander.[23] Two of these patients also had a concomitant thrush infection of the submammary fold. Hudelo and Montlaur likewise observed an interdigital thrush erosion in combination with genital localization. Engman's patient also presented lesions localized in the mammary folds, and the patient in a case to be reported here had concomitant genital and mammary thrush infection.

In the various reported cases, the diagnosis was made by finding the fairly typical mycelia and the spores in cluster arrangement in the cutaneous scrapings from these lesions and *Oidium albicans* or a closely

22. Ibrahim: Ueber eine Soormykose der Haut in frühen Säuglingsalter, Arch. f. Kinderheilk. **55**:91, 1911.

23. Alexander: Ueber interdigitale Soormykose, Dermat. Wchnschr. **73**:984, 1921; Interdigital Soormykose, Arch. f. Dermat. u. Syph. **138**:410, 1922; Beitrage zur Klinik und Diagnose der Soorerkrankungen der Haut, Dermat. Wchnschr. **75**:1125, 1922.

related organism on culture. Staheli and Lange were able to reproduce the disease experimentally by inoculation of pure cultures of the thrush fungus onto normal skin and were able to demonstrate the fungus in these reproduced lesions.

Engman, in 1920, was the first to report the localization of this fungus in the intertriginous folds beneath the breasts. His patient, a 46 year old negress, presented beneath each breast sharply circumscribed, slightly elevated, inflammatory, scaly patches and a tinea-cruris-like eruption on the genitals. Scrapings from the breast and genital lesions showed mycelial threads and sporelike bodies. Culturally, the organism was found to be the "Soorpilze" or *Oidum albicans* of thrush. Schamberg had previously mentioned a case in which the nipples of a nursing mother were apparently infected from oral thrush lesions of her infant. In Kumer's four cases of thrush infection of the breast, two occurred in nursing mothers whose infants were suffering from thrush lesions in the mouth (one of these infants also presented widespread thrush infection of the skin). Similar cases of breast infection, often in combination with lesions in the genito-anal region, have been reported by Dubreuilh and Joulia and by Alexander. In one case this last observer found in addition to genital lesions, pustular lesions over the body. From a pure culture of *Oidium albicans* obtained from these lesions, this author was able to reproduce the thrush infection experimentally.

This type of mycotic infection is for the most part observed in women with pendulous breasts. The eruption seems to be rather sharply limited to the areas of contact of the skin of the breast with the chest wall. One or both breasts may be affected. The infection is most frequently seen in nursing mothers whose infants present oral thrush infections. The primary efflorescences are pustules and small areas of scaly erythema, usually disseminated over the affected areas. The contact areas then become diffusely involved, the lesions presenting themselves as superficial scaly patches or large areas of superficial erosions surrounded by a sodden and often undermined wide epithelial border. Scattered in the vicinity of these larger plaques are many primary efflorescences of vesicles and scaling, erythematous, pea-sized areas.

Mrs. M. S., aged 58, presented beneath each breast palm-sized areas of erythema and scaling, with a central portion of superficial erosion. Surrounding the area of erosion was a wide border of sodden epidermis showing in places pinhead to lentil-sized vesicles. This area was in turn surrounded by a wider zone of erythema and scaling, and in the vicinity of this larger plaque many isolated vesicles and pea-sized areas of scaling erythema were found. Scattered over the genitals and inner sides of the thighs were isolated and confluent plaques of superficial scaling erythema with elevated polycyclic borders. Scales and the roofs of the vesicles from the breast and genital lesions revealed long,

thin, mostly unseptate mycelial threads and clusters of ovoid or round sporelike bodies. Culturally the fungus was found to be the large spore variety of *Oidium albicans*.

Thrush infection of the genital and mammary regions are not always easily differentiated from intertrigos of other origin with localizations on these areas. This is especially true of the genital and submammary intertriginous eczemas seen in diabetes. In thrush infections, however, weeping of the involved surface is rarely seen, the lesions usually presenting themselves as sharply bordered erythematosquamous plaques of geographic configuration with an elevated border of heaped-up, whitish scales, or as a membrane-like sheet of sodden epidermis which on removal leaves exposed the shiny, thin, bright red cuticle. In addi-

Fig. 3.—Intertriginous thrush infection showing lesion beneath breast.

tion, primary efflorescences of vesicles and erythema area always seen near the larger plaques. In doubtful cases microscopic examinations of scales from the lesions will establish the diagnosis. In contrast to mycotic infections, no fungous elements are found in microscopic examination of particles of epidermis from other dermatoses with localization in these areas, a fact which Kumer has proved from examination of a large number of cases.

Intertriginous thrush infection of the axilla was for a long time not known. To date there is only one such reported case in the literature. Engelhardt [24] has recently published the report of a case of thrush

24. Engelhardt: Ein Beitrag zur Aetiologie oberflachilicher Hautblastomycosen und Hautsoormykosen, Arch. f. Dermat. u. Syph. **146**:313, 1924.

infection of the right axilla combined with a typical interdigital erosion (erosio interdigitalis) due to this same fungus. In the right axilla and on the inner surface of the right arm there was a large, bright red, moist plaque covered with pustules. Mycelial threads and clusters of spores were demonstrated in the axillary and interdigital lesion. On culture the fungus proved to be *Oidium albicans* of thrush. By inoculation of culture material into normal skin of another patient, a vesicular and pustular dermatitis was provoked, and the fungus was again demonstrated in fresh preparation and culturally in this provoked eruption.

Kumer is shortly to publish the report of a second case with axillary localization.

INTERDIGITAL THRUSH INFECTION

The so-called "erosio interdigitalis blastomycetica" of Fabry [25] is but a new name for a dermatosis which has previously been reported by about half a dozen earlier observers. Ciarrocchi,[26] in 1908, under the title "Sua di una non descritta dermatose symmetrica propria del terzo interdigitale spazio delle mani," was the first observer to describe this condition. This author reported a series of cases, which, for the most part, showed an erosion in the third interdigital spaces of both hands. He gave an exact description of these lesions and reproduced in his article excellent photographs. This observer was, however, unaware of the fungous nature of the affection, and ascribed the etiology to a defect in innervation of the part.

At the June, 1914, meeting of the Berlin Dermatological Society, Madam Kaufmann-Wolf demonstrated two cases of this type of interdigital thrush infection, the patients being selected from a series of about thirty cases which she had observed during the previous eighteen months. This observer was the first to recognize the fungous nature of the erosion, having found *Oidium albicans* of thrush on microscopic examination of particles of epidermis from these lesions and on culture. During the next year this author gave a more detailed account of these cases, giving the microscopic and cultural findings and results of animal and human inoculation with the fungus. In the July, 1914, meeting of the Society franç. de dermat. et syph., Gougerot and Gancea [27] reported one case and Hudelo and Montlaur three cases belonging to this type of thrush infection.

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25. Fabry: Ueber Erosio interdigitalis blastomycetica seu sacchromycetica, München. med. Wchnschr. **64**:1557, 1917; Weitere Mitteilungen über Erosio interdigitalis blastomycetica, Dermat. Wchnschr. **66**:321, 1918.

26. Ciarrocchi: Dermatosi symetrica del terzo spazio interdigitale della mani, Gior. ital. d. mal. ven., 1908, p. 239.

27. Gougerot and Gancea: Epidermomycose due a un parasite levuriforme, Bull. Soc. franç. de dermat. et syph. **25**:335, 1914.

Gougerot and Gancea's patient presented erosions limited to the interdigital spaces of the feet and surrounding areas of the soles. In the first case reported by Hudelo and Montlaur the patient presented interdigital lesions of the feet and a concomitant thrush infection of the genital and anal regions. Their second patient showed erosions in the interdigital spaces of the right hand, and the third exhibited bilateral fourth space interdigital erosion of the feet. During the next year, 1915, Hoffman [28] reported three cases of interdigital erosion in one family, two brothers with their governess being simultaneously affected. In these various cases the fungus findings were similar to those reported by Kaufmann-Wolf. The fungus isolated from Gougerot's case was found pathogenic for the rabbit and mouse. Hudelo and Montlaur were able to cause a thrush-like lesion on the oral mucous membrane of a guinea-pig by inoculation of the fungus isolated from their first case. The fungus could again be demonstrated in bits of membrane from this oral lesion.

Fabry, in 1917, reported this interdigital erosion under the title of "erosio interdigitalis blastomycetica seu saccharomycetica." This observer's description of these lesions is identical with that given by other observers—a sharply marginated superficial erosion in an interdigital space. In his second paper, which appeared in the following year, the author chose to call the condition "erosio interdigitalis blastomycetica," which name seems to have been universally adopted. Other papers on this subject by Fabry's pupils, Berendsen [29] and Stickel,[30] soon followed. These various observers apparently did not examine particles of epidermis from these lesions but based their conclusions on cultural findings and the microscopic examination of smears from these erosions, and naturally found no mycelial filaments. This is the apparent reason for the fact that they came to the conclusion that the lesions were of blastomycetic or saccharomycetic origin—a fact which has now been conclusively disproved.

In a series of cases published by Greenbaum and Klauder in America, two types of yeasts were cultivated from these lesions—*Saccharomyces* (five times) and *Cryptococcus* (twice). These same yeasts were found as saprophytic inhabitants of the normal skin of the axilla, groin, etc. In one instance these observers were able to produce an interdigital erosion experimentally by rubbing a pure culture of *Cryptococcus* into an abraded interdigital space. These authors

28. Hoffman: Hartnackige Pilzerkrankungen der Interdigitalraume mit familiärer Uebertragung, Deutsche med. Wchnschr. **51**:1579, 1916.

29. Berendsen: Weitere Mitteilungen über Erosio interdigitalis blastomycetica, Arch. f. Dermat. u. Syph. **126**:751, 1919.

30. Stickel: Zur Frage der Erosio interdigitalis blastomycetica, Dermat. Wchnschr. **72**:257, 1921.

likewise seem to have based their conclusions on cultural findings, no report of the microscopic examination of particles of epidermis from the lesions being given in their paper.

In Mitchell's [31] reported case, microscopic examination of particles of epidermis from the lesions showed double contoured spores and numerous unsegmented mycelial threads. The fungus in this case was certainly not *Blastomyces* or *Saccharomyces*. This author was apparently dealing with the thrush or a closely related fungus.

Kumer states that he has observed more than 100 cases of this condition and that in every case he was able to demonstrate the thrush fungus in fresh preparations from the lesions and on culture. Similar microscopic and cultural findings have been reported by Lombardo, Alexander, Zingale [32] and others.

In about half a dozen cases of interdigital erosion of this type that I have examined, the fungus of thrush could be demonstrated in every case in which the lesions had not been too thoroughly cleansed before the patient's visit to the clinic. In these cases it is necessary to wait three or four days until a new collar of sodden epidermis is found at the edge of the erosions. At this time, innumerable interlacing mycelia and clusters of spores can be demonstrated. The cultures from such lesions—occasionally pure but often contaminated with various bacteria—show a fungus which cannot be differentiated from the large spored *Oidium albicans* of thrush.

These erosions are located in the interdigital spaces of both the hands and the feet. One or more spaces may be involved, on the feet all the interdigital spaces not infrequently being simultaneously affected. On the hand, the third interdigital space is the site of predilection for these erosions, this apparently being due to the increased favorability for growth of the fungus because of limitation of motion in this space. According to Kaufmann-Wolf, the space between the thumb and the index finger is never affected. The primary efflorescence is a vesicle or a group of vesicles. These vesicles soon rupture and the skin of the interdigital space becomes sodden and of a bluish tint. With exfoliation of this sodden epidermis the underlying bright red epidermic floor, which resembles raw meat, is exposed. At the border of this erosion an undermined collar of sodden epidermis and pinhead-sized vesicles are often seen. The entire lesion may be surrounded by an areola of slight scaling. These erosions may remain limited to one interdigital space for months or years, or may, by peripheral extension,

31. Mitchell: Erosio Interdigitalis Blastomycetica, Arch. Dermat. & Syph. **6**:675 (Dec.) 1922.

32. Zingale: Sulle epidermomicosi delle mani e dei piedi con speciale riferimento a due di esse descritte da Kaufmann-Wolf, Gior. ital. d. mal. ven. **64**:929, 1923.

extend along the volar surface of the metacarpophalangeal joints to involve a contiguous space. By autoinoculation, distant spaces may become involved. On the feet the eruption often spreads to involve the sides and plantar surfaces of the toes and occasionally extends onto the soles and dorsa of the feet. The condition is at times accompanied by extreme pruritus of the part, is extremely obstinate to treatment, and recurrences are frequent. This is especially true of lesions of the feet.

The condition is most frequently seen in women, and those engaged in housework seem especially prone to the infection. In the thirty cases observed by Kaufmann-Wolf, twenty-nine patients were women.

Fig. 4.—Erosio interdigitalis.

In Fabry's series of seventeen cases, thirteen occurred in the female sex, and Stickel's summary of the forty-five cases from the Dortmund clinic included thirty-eight female and seven male patients. The greater part of Kumer's 100 patients were women.

The erosion has been produced experimentally by Kaufmann-Wolf, Berendsen, Greenbaum and Klauder,[33] Pollacci, etc. Stickel, in speaking of the experiments carried out by Berendsen in the Fabry clinic, states that in seven of the eight inoculated patients an interdigital erosion

33. Greenbaum and Klauder: Yeast Infections of the Skin, Arch. Dermat. & Syph. **5**:332 (March) 1922.

fully analogous to that described by Fabry was produced. Erosions were produced in one instance each by Kaufmann-Wolf and by Greenbaum and Klauder. Alexander, on the other hand, reports entirely negative results. This observer states that after long and painstaking experiments with cultures obtained from his own cases of interdigital erosions and with cultures sent to him by Fabry, he was not able to produce a typical interdigital erosion in a single instance.

THRUSH INFECTIONS OF THE NAILS

Few cases of this type of thrush infection have been reported. There is little similarity among the various reported cases, some being characterized by the formation of abscesses beneath the nail wall (Dubendorfer,[34] Frei,[35] Kumer), others by hyperkeratotic changes in the nails (Forbes,[36] Pellier, Lombardo, Guggenheim,[37] etc.). From the few reported cases it is difficult to answer the question as to whether the thrush fungus is the cause of these nail changes or is found as a mere secondary saprophytic invader in already altered nails. In spite of this limited material, one is convinced, on reading the literature, that thrush infection of the nails really exists. Up to the present time, such lesions have not been produced experimentally; yet few inoculation experiments have been reported. Guggenheim was able, in one instance, to cause an onychia on the claws of a guinea-pig by inoculation of culture material obtained from his case of nail involvement.

Forbes' case, that of a 3½ year old child, presented a thrush infection of the mouth and onychia of the right first and third fingers and left thumb, characterized by atrophy and heaped-up hyperkeratotic masses on the nails. The thrush fungus was demonstrated microscopically and culturally in the mouth and nail lesions.

Pellier [38] observed a 54 year old man with bilateral onychia of the large toes. The nails were lusterless, opaque, yellowish, friable, and presented irregular, heaped-up keratotic masses. The microscopic examination of nail particles treated with dilute potassium hydroxid solution revealed mycelial threads and round or ovoid cell-like bodies.

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34. Dubendorfer: Ein Fall von Onychomycosis blastomycetica, Dermat. Zentralbl. **7**:290, 1904.

35. Frei: Ein Soormykose der Nagel bei einer Salvarsan Dermatitis, Arch. f. Dermat. u. Syph. **129**:404, 1921.

36. Forbes: Meeting of Dermatological Section of Royal Society of Medicine, June, 1909, Brit. J. Dermat. **21**:221, 1909.

37. Guggenheim: Ueber Onychomykosis oidiomycetica, Arch. f. Dermat. u. Syph. **142**:308, 1923.

38. Pellier: Sur une nouvelle forme parasitaire des onychomycoses, Ann. de dermat. et syph. 1912, p. 563.

Plants of nail particles on various mediums gave almost a pure culture of the fungus. This was identified by Vuillemin as closely related to the fungus of thrush.

Dubendorfer's case presented redness and swelling of the nail walls and small subungual abscesses. From these abscesses a blastomyces was obtained in pure culture. It seems probable, from the description of this fungus, that this observer was dealing with the organism of thrush.

In the course of an arsphenamin dermatitis Frei observed the development of acute onychia of several fingers and toes with subungual abscesses in the region of the lunula of the affected digits. Numerous mycelia and clusters of spores were found in these abscesses, and the fungus of thrush was grown in pure culture from the pus. A similar case, in which the thrush fungus was demonstrated microscopically and culturally in the pus of subungeal abscesses, was described by Kumer.

In Guggenheim's patient all the nails of both hands were opaque, lusterless, thickened, and the surface irregular from deep furrows and heaped-up keratotic masses. In places the nails were elevated from their beds and the intervening space filled with heaped-up, horny material. Microscopic examination of nail particles revealed mycelia and spore-like bodies, and on culture the fungus was identified as *Oidium albicans*. By inoculation of a pure culture of this fungus onto the claws of a guinea-pig, similar keratotic changes were provoked.

Lombardo has reported two cases of thrush infection of the nails in association with a similar infection of the oral cavity and glabrous skin, one case also presenting a paronychia of the left index finger which was apparently due to this fungus. *Endomyces albicans* was demonstrated microscopically and culturally in the various skin, oral and nail lesions. Staheli and others consider the case reported by Bourgeois [39] as an example of thrush infection of the nails.

OTHER TYPES OF THRUSH INFECTION

Lombardo has recently described a widespread infection of the skin and mucous membrane of the mouth in an 18 year old patient, and from the microscopic and cultural demonstration of *Endomyces albicans* in the various cutaneous and oral lesions, this observer is of the opinion that the eruption is due to the thrush fungus. The eruption on the skin appeared as large crusted and squamous plaques resembling a widespread impetigo. Membranous lesions of the mouth, perlèche-like lesions of the lips, onychia of the thumb, index and middle fingers of the right hand and paronychia of the left index finger developed. Mycelia and

39. Bourgeois: Ueber Onychomykosis saccharomycetica, Dermat. Ztschr. **22**:411, 1915.

clusters of spores were demonstrated in the various skin, mouth and nail lesions. Histologic specimens from the skin lesions showed numerous mycelial filaments as low down in the epidermis as the malpighian cells. Culturally, the fungus was identified as *Endomyces albicans* (*Oidium albicans*) of thrush. Inoculation of animals and infants (2) gave positive but rather short lived eruptions.

Tanner and Feuer,[40] in America, report a case in which there were 5 to 10 mm. sized ulcerative lesions on the left index finger, of some years' duration. *Endomyces albicans* was grown in pure culture from pus discharged from these lesions. No microscopic examination of the pus from these lesions is reported in their paper. The paper loses worth because the thrush fungus is occasionally found as an undesired contamination in dermatoses of other origin, especially in pus infections (Kumer, in a case of abscesses in a tuberculosis cutis; Alexander, in a deep tinea barbae; Frei, in a case of arsphenamin dermatitis, etc.).

In summarizing the various cases of thrush infection of the skin, we find that the primary efflorescences and the mode of formation of larger plaques are the same. The various types, exclusive of the interdigital thrush infection, respond readily to therapeutic methods causing exfoliation of the epidermis, (Whitfield's and Wilkinson's ointment, iodin, etc.), while some of the thrush lesions, as that observed in the water-bed treatment, often heal spontaneously. In innumerable instances, several different types of this infection were observed in the same patient, as simultaneous breast and genital infection or an interdigital erosion with concomitant oral and body lesions in nursing infants, etc. The majority of cases reported displayed two or more types of the infection, or better, two or more localizations of this same dermatosis. Familial infection has been reported by Hoffmann, and Kumer observed an epidemic due to this fungus. These facts speak for a common etiologic factor.

The criterion for this is, however, the finding of the thrush fungus in the fresh preparation (as in scales, roofs of vesicles) from these various lesions. Control experiments show that on normal skin and in various dermatoses of nonmycotic origin, as eczema, no mycelia or clusters of spores can be found. There is apparently only one case in the literature (Frei) in which, in the course of a moist and crusting arsphenamin dermatitis, mycelia and clusters of spores of the thrush fungus could be demonstrated microscopically in skin particles, the fungus apparently existing here as a pure saprophyte. To make a diagnosis of thrush infection it is necessary to find the mycelial threads

40. Tanner and Feuer: Culture Studies on an Infection of the Skin by Endomyces Albicans, Arch. f. Dermat. u. Syph. **38**:365, 1920.

and groups of spores in cluster-like arrangement. And these are usually more numerous than in any other type of fungus infection, at times veritable masses of interlacing mycelia and clusters of spores being found. A single fragmental mycelium or isolated spore or cell-like body is not sufficient to warrant the suspicion that the fungus is the cause of the dermatosis. These mycelial filaments present such a characteristic appearance that with a little practice they can readily be differentiated from the mycelia of other fungi. They are long, thin, mostly unseptate, exhibit little branching, and show short lateral and side budding.

Of further yet less value is the cultural demonstration of the fungus in such lesions. One occasionally gains from a plant from normal or diseased skin an isolated thrush colony as an unwished-for contamination. In thrush infections, the culture is always markedly positive, colonies growing from every plant and usually in such profusion on maltose-agar that one can speak almost of a pure culture. These appear from four to six days after inoculation of the medium as pinhead-sized white or slightly yellowish hemispherical colonies. After from three to four weeks peripheral growth ceases, individual colonies rarely attaining a size greater than 1 cm. in diameter. The central portion of these colonies is usually elevated, yellowish or cream color, and surrounded by a lighter, flatter zone. The younger colonies show no growth in filamentous form, yet in older cultures a fine filamentous areola surrounds the colonies and extends out into the surrounding medium. Younger colonies, except on special mediums, usually appear as a pure yeastlike growth of round and ovoid cells. In older cultures (four or five weeks old) long, thin, simple and branched mycelia with here and there side budding and clusters of spores, either free or attached to the mycelia, are seen. The culture tubes have the characteristic odor of fermentation, and gelatin is liquefied.

The exact botanical position of this fungus is still a matter of much contention. This is the ground for the numerous names by which thrush infections have been labeled, as oidiomycosis, endomycosis, saccharomycosis, etc. Fabry speaks directly of an erosio blastomycetica. The reason for this, as previously stated, is that this observer examined only smears from these interdigital lesions and not scales and particles of the sodden epidermis. He necessarily found no mycelial elements, so he came to the conclusion that he was dealing with an organism belonging to the *Blastomyces* group.

Biologic reactions, such as specific skin tests found in *Trichophyton*, *Microsporon* and favus infection, and the agglutination phenomena have proved of little value, apparently because this fungus grows in the superficial layers of the skin, thereby exciting no antibody formation. In cases of thrush infection of the skin, as in cases of superficial herpes

tonsurans infection, a specific skin test from the intradermal injection of a thrush vaccine is not to be expected. By repeated intravenous injection of culture material into animals, an agglutinating serum against the thrush fungus can be provoked, yet the titer is usually very low (reaches hardly 1:80) and does not agglutinate all varieties of the thrush fungus. In a case of interdigital thrush infection, Kaufmann-Wolf found that the patient's serum agglutinated the thrush fungus in a dilution of but 1:20 to 1:80. Kumer, on the other hand, reports wholly negative agglutination experiments in cases of water-bed and interdigital thrush infection.

CHRONIC PARONYCHIA DUE TO THE FUNGUS OF THRUSH (?)

Kumer, in 1921, reported a series of twelve cases of chronic paronychia which he concluded—from microscopic examination and cultural studies of the lesions—were in all probability due to the thrush fungus. These cases presented chronic paronychias of the fingers characterized by a bolster-like swelling of the nail wall and secondary changes in the nail itself. In one of these cases, the author found, on examination of the nail and nail wall lesions, mycelial threads and clusters of ovoid or round highly refractile spores. On microscopic examination of the paronychial lesion in the eleven remaining cases, round and ovoid highly refractile sporelike bodies were found. Typical mycelia could not be demonstrated in fresh preparations in these cases. The fungus obtained on culture in all twelve cases could not be differentiated from the large-spored, gelatin-liquefying variety of *Oidium albicans*. One of Kumer's cases, six months after the beginning of the paronychial condition, presented a typical interdigital thrush infection (erosio interdigitalis).

Volkmann [41] has observed three examples of this type of paronychia in nurses, and Tillman [42] has reported two similar cases, one case being cured by surgical removal of the nails of the affected fingers and the second by the application of a 10 per cent. sulpho-ichthyolate salve. More recently, Holbert [43] presented such a case at a meeting of the Silesian Dermatological Society in Breslau.

I have had the opportunity of studying five cases of this type of paronychia, the clinical picture, microscopic and cultural findings being similar to those originally reported by Kumer.

This paronychia is characterized by a peculiar bolster-like inflammatory swelling of the nail wall and secondary dystrophic changes in the nail itself. The nail wall shows an inflammatory cylindrical swelling in

41. Volkmann: Ueber eine besondere Form der chronischen Paronychie (zu der Arbeit von Kumer), Mitt. a. d. Grenzgeb. de Med. u. Chir. **33**:662, 1921.

42. Tillman: Bermerkung zur Arbeit Kumer (ch. paronychie), Mitt. a. d. Grenzgeb. d. Med. u. Chir. **34**:596, 1922.

43. Holbert: Meeting Silesian Dermatological Society, Breslau, June, 1923

its entire circumference and such that a cross-section through the swelling would appear as a half or three quarter circle. The most marked swelling is found in the region of the lunula, gradually decreasing toward the finger tips. The skin of the swollen nail wall is thin, glistening and without the normal, superficial markings. The nail fold in the region of the lunula is usually gaping, and the free edge of the nail wall in this region is fissured and often shows small crust formations. On pressure over the area of most marked swelling, a seropurulent secretion can be expressed from the region between the nail wall and the nail. This paronychial inflammatory swelling is usually sharply differentiated from the normal surrounding skin.

The nail changes are of purely secondary character and depend on the duration and intensity of the paronychial condition. In early cases the nails of the affected fingers are of normal appearance, but in cases of longer duration the nails are thickened, the surface lusterless and marked by transverse furrows. The nail in its distal portion is often elevated from its matrix, and the intervening space filled with a keratotic epithelial mass.

The paronychia at first is usually localized to one finger; gradually other fingers become involved, and in the course of months (occasionally years) practically all the fingers of both hands may be similarly affected.

Details as to the beginning of the inflammation are lacking, the patients usually presenting themselves at the clinic after the condition has existed for some weeks or months. All the patients relate that the condition began with slight sticking pain, redness and marked swelling of the nail wall in the region of the lunula. This swelling extended gradually, but uniformly, around the sides of the nails to gain the finger tips. In the course of weeks or months, neighboring fingers became involved, or the condition spread to involve fingers of the other hand. In three of Kumer's series and in one of my cases, a single finger was involved. In several of Kumer's cases, marked pain in the affected part was experienced. In only one of my cases was pain a prominent symptom, and then it was of short duration.

A further characteristic of this paronychia is the chronic course of the condition and its recalcitrancy to treatment. These patients relate that for months and even years they have been treated by various physicians and in various clinics with salves, wet dressings, plasters, the roentgen ray and quartz lamp rays, but without improvement. One of my patients had even undergone surgical removal of the nails, which seemed to exaggerate rather than benefit the condition.

The cases thus far reported have occurred in females, for the most part in middle-aged women engaged in housework. While one of my patients attributed her affection to the manicurist, three others were of the belief that the inflammation was caused by continual exposure of

the hands to soapy water while scrubbing or washing. Two of Kumer's patients attributed their condition to injury of the nail wall received at the manicurist's, one of these patients relating that she did not dare practice the slightest care of the nails, since the most superficial injury to the nail wall was always followed by paronychial involvement of that finger.

REPORT OF CASES

Case 1.—A. B., a woman, aged 53, had characteristic swellings of the right index finger and left thumb. The condition of the index finger began fourteen months previously. There was no exact history of onset. Six weeks previous to her initial visit to the clinic, the nail wall of the left thumb suddenly became swollen, red and painful. During the first three days, the pain was so intense that the patient was unable to sleep. After eight days of subjective pain, the symptoms disappeared, but the redness and swelling persisted. When viewed six weeks later, both fingers showed the characteristic bolster-like inflammatory swelling of the nail wall. The nail of the right index finger showed secondary dystrophic changes of the surface, and the distal portion of the nail was elevated from its matrix, the space being filled with a yellowish, horny mass. The nail of the thumb was of normal appearance.

Case 2.—E. N., a woman, aged 35, a cook, had had the condition for six months. The patient said that it followed injury received when manicuring the nails. The nail wall of the right index finger showed typical swelling with secondary changes in the nail similar to those in Case 1. For the last seven weeks there had been involvement of the right middle finger. This finger presented typical paronychia but no nail changes. The patient said that she had had a similar condition on the thumbs eighteen months before. Inflammation disappeared spontaneously after six months.

Case 3.—C. L., a woman, aged 35, whose occupation was housework, had paronychial swellings which began six months previously with involvement of the left thumb. In the course of two months, the left second, third, fourth and fifth and all fingers of the right hand became involved. On pressure over the swelling of several fingers, seropurulent exudate could be expressed from the fold between the nail and nail wall. The nails of all the involved fingers showed marked secondary changes.

Case 4.—H. P., a woman, aged 52, whose occupation was housework, had had the condition for six months. The right index finger showed typical paronychial swelling with marked changes in the nail. The patient said that the right middle finger was similarly involved two years before. Spontaneous healing occurred after eight months.

Case 5.—M. A., a woman, aged 40, whose occupation was housework, had paronychial swellings which began three years before with involvement of the left ring finger. Three months later the left middle finger became similarly affected. Within the next year, the right ring and left index fingers became involved. One year ago, the nails of the left third and fourth fingers were removed surgically. There was no benefit from this treatment. At the time of the initial visit to the clinic, the patient presented typical paronychia, with marked nail changes of the four fingers mentioned.

In all cases the microscopic examination of nail particles taken from the portion of the nail covered by the paronychia and of bits of epidermis taken from the under surface and free edge of the nail wall showed innumerable round and

ovoid, highly refractile, yeastlike bodies. These spores or sporelike bodies were not arranged in clusters, but scattered through the specimen prepared with potassium hydroxid. Typical mycelial filaments could not be found, only an occasional short unseptate fragment which could not with certainty be identified as a true mycelial thread. In secretion from the lesions yeastlike bodies were found. These were likewise diffusely scattered through the specimen and not arranged in clusters or groups.

As was expected, cultures from nail particles, bits of epidermis from the nail wall and from the seropurulent secretion of the paronychia, gave on agar-agar micro-organisms of various kinds, especially staphylococci. On maltose agar such a prolific growth of the thrush fungus was obtained that often bacteria and the

Fig. 5 (Case 3).—Paronychial swellings.

ordinary molds seemed to play a secondary rôle. In two of the five reported cases pure cultures of the thrush fungus was obtained from plants of nail particles and scales.

These colonies usually make their appearance from four to six days after inoculation of the culture tubes; at this time a pinhead-sized, round, hemispherical, slightly yellowish colony appears. These colonies extend peripherally, usually retaining the round form for a period of about three weeks, after which time they cease to grow peripherally. On ordinary tubes individual colonies rarely attain a size greater than 1 cm. in diameter. The centers of these colonies are usually elevated,

yellowish and surrounded by a lighter, flatter zone. The surface is either flat or slightly wrinkled. At times the entire area seems to be composed of a mass of minute juxta-opposed, smaller colonies. The younger colonies show no filamentous growth, but in older cultures a fine filamentous areola is seen to surround the colonies and extend out into the surrounding medium. From cultivation on various mediums it was found impossible to separate this fungus from the large spore variety of *Oidium albicans*—the fungus liquefies gelatin, and the culture tubes give the characteristic odor of fermentation. In younger colonies the growth was purely of yeastlike character—round or oval cells which increased rapidly through budding. In older cultures (from five to eight weeks), long, thin, simple or branched mycelial threads with here and there lateral budding, and clusters of spores, either free or attached to the mycelia, were found.

Kumer found the thrush fungus isolated from these paronychia pathogenic for the dog on intravenous injection and usually lethal for white mice on subcutaneous or intraperitoneal injection. The same observer reports negative results in two instances in which he attempted to cause a paronychia on the fingers of patients by rubbing a pure culture of the thrush fungus, isolated from this type of chronic paronychia, into the under surface of the nail wall.

I carried out experiments on myself with staphylococci and thrush fungi cultured from the cases of chronic paronychia mentioned above. In all instances the same procedure was followed: the nail and surrounding skin was disinfected with alcohol and iodin, the cuticle in the region of the lunula elevated from the nail, and a superficial abrasion caused on the under surface of the nail wall. In three instances pure cultures of staphylococci were rubbed onto the surface of this abraded area by means of a platinum loop. In all instances the results were absolutely negative, no signs of inflammation appearing at the site of inoculation. In a fourth instance a pure culture of the thrush fungus was rubbed into the under surface of the nail wall as in the three foregoing experiments. After twenty-four hours, the nail wall in the inoculated area became red, swollen and slightly painful to pressure. After four days, the swelling of the nail wall had reached its maximum, the condition now appearing as an acute paronychia, the only difference being that in this case the surface of the swelling was studded with minute pin-point vesicles. Cubital and axillary glands became swollen and painful. Signs of the inflammation then began to subside, and by the end of two weeks the nail wall showed a normal contour. Desquamation of the epidermis over the area of inflammation then followed. The experiment was considered negative, so no cultures were made. The inoculation was not repeated.

TREATMENT

The extreme resistance to treatment in these cases has already been mentioned. Salves, wet dressings, quartz lamp therapy, etc., were without avail. In this clinic the only satisfactory results have been attained from radium treatment, by which means complete healing of the lesions is usually effected. A cured case of this condition is pictured in the book by Rhiel and Kumer on "Radium and Mesothorium Therapy."

That the thrush fungus is the cause of these paronychias has to the present time not been definitely proved. The rather constant clinical picture which these lesions present, gives the impression that they have a common etiology. That such prolific growtl. of the thrush fungus can be obtained on culture does not seem to be a mere coincidence, and in other conditions of the nail and the nail wall, only an occasional thrush colony could be obtained on culture.[44]

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44. Since the completion of this article a paper on "Mycotic Paronychia and Dermatitis" by Dr. Kingery and Dr. Thienes has appeared in the Arch. Dermat. & Syph. **11**:186 (Feb.) 1925.

MYCOSIS FUNGOIDES

ITS RELATION TO LEUKEMIA AND LYMPHOSARCOMA *

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In view of recently reported cases of mycosis fungoides showing the histologic picture of lymphosarcoma, it seems opportune to record two additional instances, particularly since one of them has to do with the relationship between mycosis fungoides and lymphatic leukemia.

CASE 1.—H. L., a man, aged 42, married, a cabinet maker, was in good health until April, 1920. At that time a scaling, itchy eruption appeared on the palms, that eventually spread to the trunk and extremities. About two years later, raised, circular swellings occurred on the forehead, scalp and thighs. On July 14, 1922, the patient was admitted to the Dermatologic Clinic of the University and Bellevue Hospital Medical College. He said that he had previously visited several other institutions, and had received roentgen-ray treatment, without beneficial results.

The cutaneous picture, on the day of his admission, was that of a generalized eruption which consisted of areas of erythema with fine scaling. In localized foci there were erythematous, slightly raised, infiltrated plaques, with sharply demarcated borders. These plaques ranged in size from 1 to 3 cm. and were usually of irregular shape; but in some places they had a circular or semicircular outline. There was a rounded, nodular growth on the right temporal region that measured 4 cm. in diameter and 1.5 cm. from base to summit. The inguinal lymph nodes were enlarged to the diameter of about 3 cm. The blood count was normal.

After a few roentgen-ray treatments, the patient discontinued his visits to the clinic. He was admitted to the Lincoln Hospital, Oct. 24, 1922. Physical examination on admission showed that the chest and abdomen apparently were normal. There was a generalized erythematous, scaly eruption in the skin and many irregularly shaped red or reddish-purple elevated patches with well defined borders. Some of the lesions were lichenoid, others showed ulceration with serous oozing and crusting. In addition there were numerous nodular growths scattered over the body, ranging in size from a few millimeters to 3 cm. They were firm and were not tender to the touch. Many of them were broader at the free end than at the base. Examination on Nov. 2, 1922, revealed that the spleen was enlarged and palpable to a depth of 3 cm. beneath the costal margin. The blood count on the same date revealed: hemoglobin, 75 per cent.; red blood cells, 3,600,000; white cells, 34,000; lymphocytes, 88 per cent.; polymorphonuclears, 12 per cent. Urinanalysis revealed a trace of albumin and a few hyaline and granular casts. The patient died from pneumonia, Nov. 12, 1922. Permission for necropsy was not obtained.

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Comment.—We have for consideration a case which for a period of nearly two years ran a course corresponding to the usual clinical picture of mycosis fungoides. A primary eczematoid dermatosis was succeeded by the appearance of infiltrated erythematous plaques in the true skin. This stage was followed at the end of two years by enlarged lymph nodes and generalized ulcerating cutaneous and subcutaneous nodules. Shortly before the patient's death the additional phenomena of enlargement of the spleen and the blood picture of lymphatic leukemia

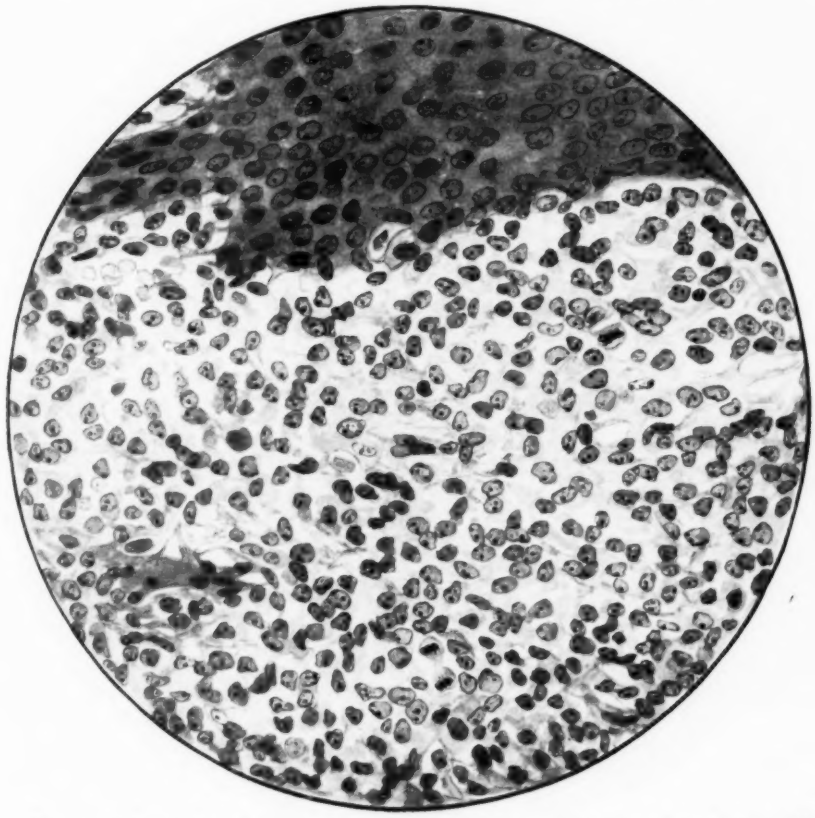

Fig. 1 (Case 1).—Section from a cutaneous nodule showing large cells (reticulum type) of a uniform variety. Tumor cells in mitosis.

developed. The histologic picture (Figs. 1 and 2), together with the clinical features, which are identical with those described by Kaposi under the heading of lymphoderma perniciosa, suggest that Kaposi's case should not have been recorded as a clinical or pathologic entity, but as an example of an unusually malignant type of mycosis fungoides. Support for this view is to be found in the work of Vidal, Hallopeau and

Paltauf, all of whom regarded Kaposi's lymphoderma perniciosa [1] as a form of mycosis fungoides.

THE DEVELOPMENT OF A LEUKEMIC BLOOD PICTURE IN MYCOSIS FUNGOIDES AND RELATED CONDITIONS

A leukemic blood picture in mycosis fungoides seems to be rare. Fordyce,[2] out of a wide experience, has not encountered such a case in ten years. There are cases in the literature, however, showing terminal

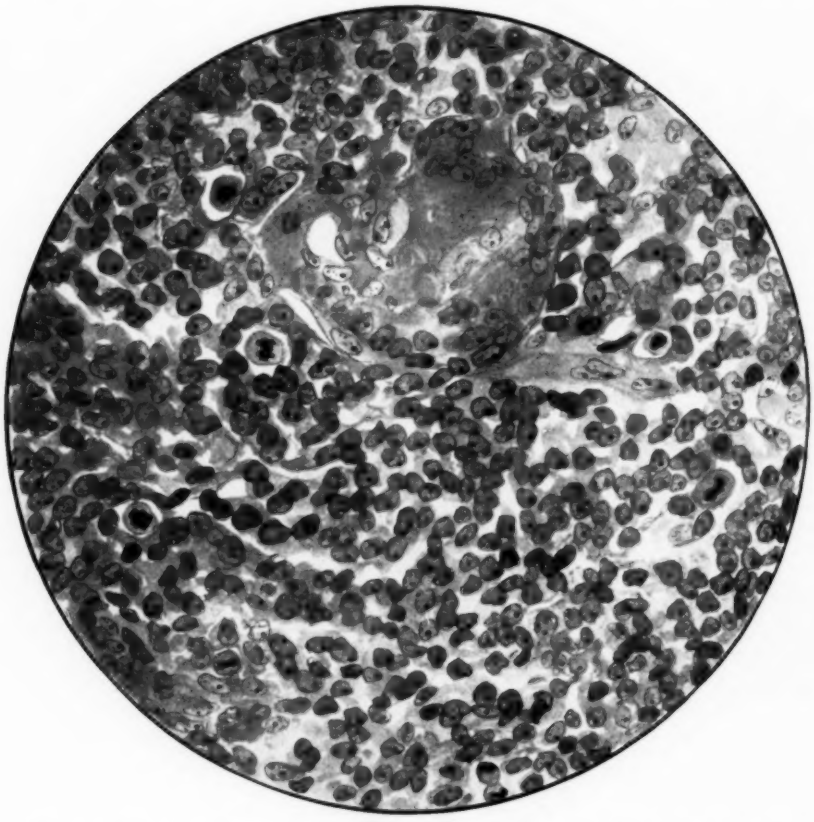

Fig. 2 (Case 1).—Same as Figure 1, from a field farther down, showing same type of cells, numerous mitoses and a foreign body giant cell.

lymphatic leukemia. For example, Pardee and Zeit [3] reported a case of mycosis fungoides that developed the picture of lymphatic leukemia

1. Pathology and Treatment of Diseases of the Skin, New York, William Wood & Co., 1895.

2. Fordyce, John A.: Personal communication.

3. Pardee and Zeit: J. Cutan. Dis. **29**:7, 1911.

shortly before death. Pelagatti [4] has observed similar cases, and recently Symmers [5] described a case of lymphatic leukosarcoma from Bellevue Hospital in which the leukemic blood picture appeared three weeks before death. Alexander Fraser [6] has observed the same phenomena in cases of lymphosarcoma in the South American red squirrel. In these squirrels lymphosarcoma (Fig. 3) occurs spontaneously and can

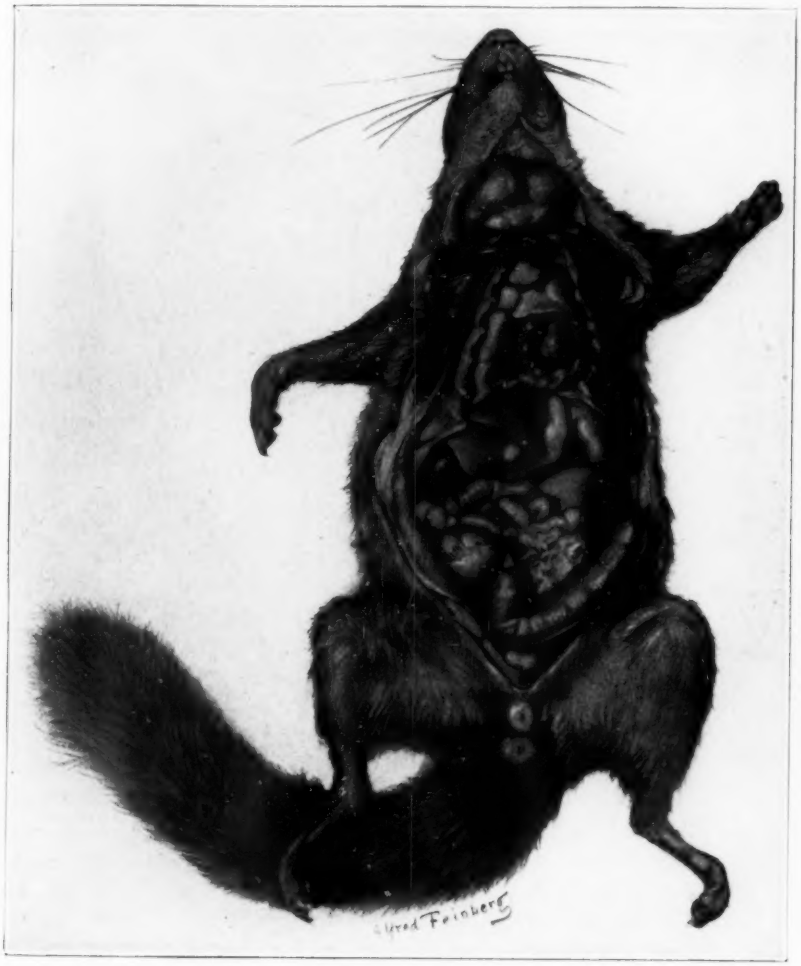

Fig. 3.—Lymphosarcoma in a South American red squirrel, showing involvement of salivary glands, lymph nodes and liver.

4. Palagatti, quoted by Nanta: Ann. de dermat. et syph., Ser. 5, No. 3, pp. 572, 639, 694, 1912.

5. Symmers, Douglas: The Association of Certain Cutaneous Lesions with Diseases of the Hemoipoietic System, J. Cutan. Dis. **37**:1 (Jan.) 1919.

6. Fraser, Alexander: Personal communication.

be transmitted to healthy animals of the same species by transplantation of the tumors or subcutaneous injection of emulsified tumor tissue. The disease begins with the development of tumors in the orbit, salivary glands, lymph nodes, thymus and sometimes in the intestines, and remains as tumors without blood metastasis until shortly before death when the blood becomes flooded with tumor cells, thus duplicating the picture of leukosarcoma as encountered in man. The cells in these tumors are always of the large reticulum type (Fig. 4). An interesting

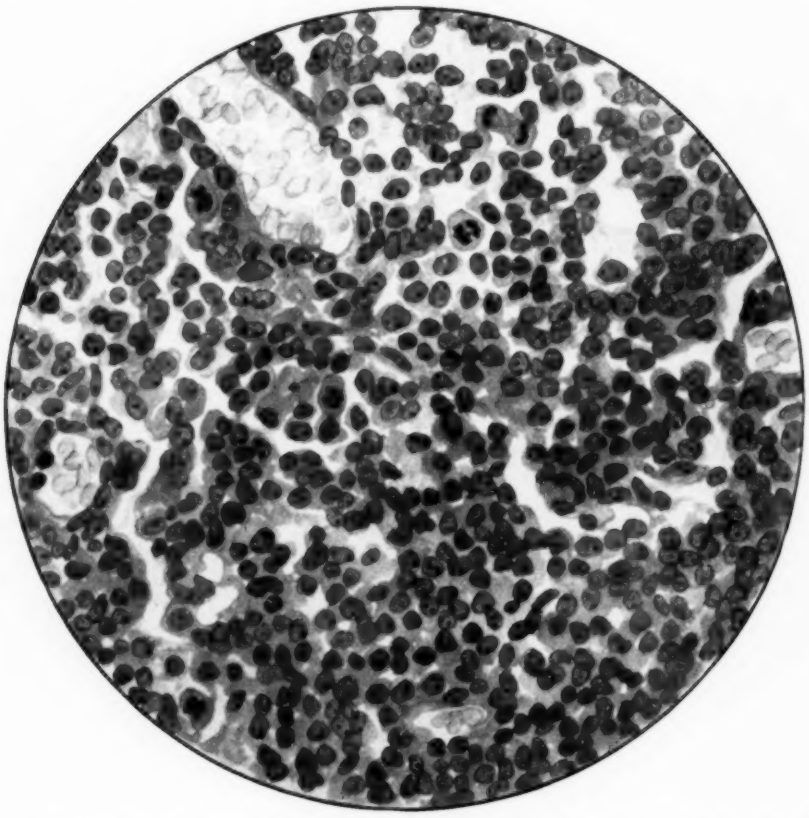

Fig. 4.—Section from lymph node of squirrel, showing same reticulum type of cells as in Figures 1 and 2. Tumor cells in mitosis.

fact is that the tumors occasionally undergo spontaneous resolution as sometimes occurs in lymphosarcoma in man.

A great deal has been written relating to the complicated problems involved in the pathogenesis of leukemia. Reitano[7] discusses the part played by the reticular tissue in the formation of leukemic blood and

7. Reitano, D.: Grado e significato clinico della participazione del tissuto istivide alle formazione, Riforma med. **39**:553, 1923.

describes the differential features between the histoid (reticular) and parenchymatous elements. He concludes that the reticular participation is directly proportionate to the acute character of the pathologic process. Ewald [8] reported a case which he designated leukemia reticuloendotheliosis, and pointed out that the so-called acute leukemias are now commonly considered as symptomatic manifestations of sepsis. Martinotti [9] applies the term hemoblastosis to a series of leukemic processes in which he includes mycosis fungoides, pernicious lymphoderma, and related conditions. Zurhelle [10] expresses the belief that the capacity

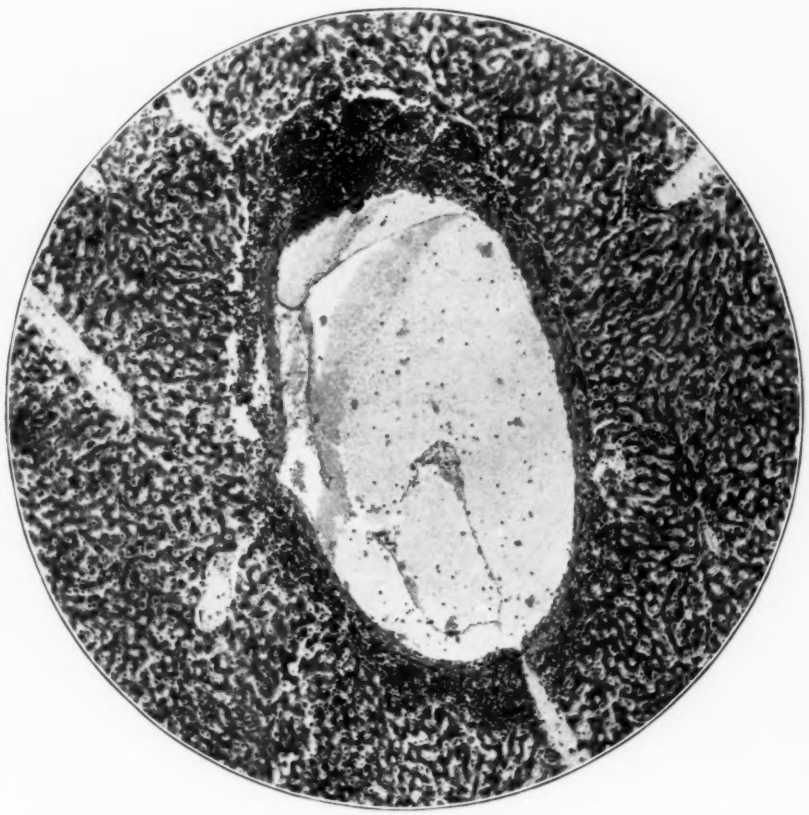

Fig. 5.—Section of squirrel's liver showing sinusoides filled with tumor cells. Infiltration of wall of central vein. Cells breaking into lumen. (Low magnification.)

8. Ewald, O.: Die leukämische Reticuloendotheliose, Deutsch. Arch. f. klin. Med. **142**:222, 1923.

9. Martinotti, L.: Le manifestations cutani nelli emoblastosi, tumori **8**:63, 1922.

10. Zurhelle, E.: Ueber Hauterscheinungen bei Erkrankungen des myeloischen Systems; myelogene Leukämie, Chlorome, Myelome, Deutsch. med. Wchnschr. **482**:1610, 1922.

of differentiation originally belonging to the cells of the vascular wall is aroused in the skin more frequently than is commonly recognized. If this view is correct, we have an explanation for the occurrence of both lymphatic and myelogenous leukemic changes in the skin independent of the theory of invasion of cellular elements from the bone marrow in the case of myelogenous leukemia, and from the lymph nodes in lymphatic leukemia. Lack of data (there was no opportunity for postmortem examination) precludes an interpretation of the leukemic process in the present case. In the case of the squirrels, however, the histologic picture showing infiltration of the blood vessels with tumor cells (Fig. 5) and the absence of pathologic change in the bone marrow would seem to justify the interpretation of the leukemic picture in these animals as the metastasis of tumor cells to the blood stream.

The following case is recorded as presenting the characteristic clinical features of mycosis fungoides which at necropsy showed the morphologic picture of lymphosarcoma.

CASE 2.—A woman, aged 40, a Czechoslovakian, admitted to the Bellevue Hospital, March 3, 1925, was said to have had a skin lesion at 4 years of age, and one at 22 lasting several months after the birth of her first child. She had had four healthy children and no miscarriages. Venereal diseases were denied. Some time before the birth of her youngest child, now 3 years of age, she began to show skin lesions on the face and head, and a lump appeared in the right axilla. Several physicians who were consulted had prescribed ointments, and one probably gave extensive roentgen-ray treatments. The patient was a fairly well nourished white woman. Shortly after admission she was seen in consultation by Dr. Douglas Symmers, who made the clinical diagnosis of mycosis fungoides. There were a few areas on the head on which hair was growing, but over most of the frontal, right and left parietal regions there was none. Where there were no open lesions, there were thin, noncontracted scars without sign of hair growth. The eyebrows and eyelashes were intact. Over the forehead, temples, most of the head, the right side of the face and neck were crusted, rounded, punched-out lesions, without much induration. Removal of the crust left an oozing surface; there was no retraction of the scars. Over the breasts and folds beneath them and in the lower folds of the abdomen were curved linear almost circoid lesions not at all deep, 5 to 7.5 mm. wide and from 5 to 10 cm. long. The skin immediately beneath the breasts on the upper anterior abdominal wall presented a pinkish, glistening erythematous patch, suggesting the so-called homme rouge appearance. The lymph nodes in the right inguinal region were moderately enlarged, firm and discrete. The axillary and inguinal groups seemed confluent and from 8 to 14 cm. in diameter. The lymph nodes above and below Poupart's ligament on the left side were not so large as on the right. The temperature varied from 97.6 to 104.4. The Wassermann test was negative. On March 26, 1925, the blood contained: white blood cells, 42,100; polymorphonuclears, 98 per cent.; red blood cells, 4,430,000; on April 3, 1925: white blood cells, 54,550; polymorphonuclears, 97 per cent.; red blood cells, 3,090,000; hemoglobin, 70 per cent. A portion of skin taken from the edge of an ulcerating lesion was submitted to Dr. Symmers, who reported that the microscopic appearances were those of lymphosarcoma (Fig. 7). The patient died on April 3, 1925, at 11 p. m.

Necropsy.—Necropsy was performed by Dr. Douglas Symmers, director of laboratories, Bellevue Hospital.

The body was that of a woman 40 years of age, 168 cm. in length, of large, well developed frame, fairly good musculature and nutrition. On the right side of the head, occupying the region of the dome of the parietal bone, was a plaque-like lesion, which was elevated about 3 cm.. This was somewhat T-shaped, and the edges gradually sloped off into the tissues of the surrounding scalp, which, in this region and, in fact, throughout the head, was practically bereft of hair. Just

Fig. 6 (Case 2).—Erythematous patches and ulcerated lesions on trunk, neck and scalp.

above the ear on the right side was a somewhat triangular shaped, plaque-like lesion, which was likewise elevated for a distance of about 3 mm.; the upper edge of the plaque, corresponding to the base of the triangle, shaded off gradually into scalp tissue, while at the edges of the two other sides of the triangle were large, scablike, ulcerated areas, which were fairly sharply demarcated from the surrounding tissues. On the right side of the forehead, commencing just below

the hair line and extending upward and inward toward the midline of the skull, was a large ulcerated area, the edges of which were rounded and elevated, the base granular and brownish red. This area measured about 7 by 3 cm. On the left side of the forehead, just above the outer angle of the eye, was a large, irregularly outlined, deeply ulcerated area, covered by a brownish-red scab, the edges elevated, rounded and gradually sloping off into the adjacent tissues. The anterior and lateral aspects of the neck presented numbers of discrete and confluent depressed, scarlike areas, with elevated, rounded edges. On the anterior surface of the left chest, in front of the axillary fold, was a large, irregularly outlined, deeply ulcerated area, the edges of which were indurated, in places rounded, in other places extending into the surrounding skin in the form of indurated plaques. A similar area was present on the right breast surrounding the nipple. On the anterior surface and inner aspect of the right breast, near the midline, was an elevated, oval area, measuring 3 by 2.5 cm. and raised above the surface to the extent of 0.5 cm. The nodule was rather soft in consistency, and the skin covering it was dirty pinkish, and in places it was somewhat scaly. The lymph nodes in the right axilla were markedly enlarged, firm and discrete, while just in front of the right axilla, extending inward and downward, was a fist-sized, oval swelling, which apparently represented an extension of lymph node enlargements from the axillary space. Almost the same description applies to the lymph nodes in and in front of the left axilla. The cervical nodes were markedly enlarged, firm, discrete and freely movable. The skin covering practically the whole of the left breast, but particularly marked immediately around the nipple, presented a dirty bluish appearance and was thickened and in places scaly. Over the anterior abdominal wall, just beneath the breasts and extending almost as low as the umbilicus, from one side to the other, were fifteen or sixteen irregularly outlined, superficially ulcerated areas, the edges of which were indurated. The skin immediately beneath the left breast on the upper anterior abdominal wall presented a large, pinkish, glistening, erythematous patch. The lymph nodes in the right inguinal region were moderately enlarged. On section, the intact nodule above described showed a smooth, cream colored, glistening surface, the whole resembling the cut surface of a lymph node. No thymic remains were visible, but in the region of the thymus and around the trachea were innumerable discrete, firm lymph nodes, varying in size from 0.5 to 2 cm. On section, most of them were markedly congested; others showed whitish areas alternating with congested portions.

The spleen measured 18 by 9.5 by 6 cm. and weighed 675 gm. Seen through the capsule, it presented a light reddish appearance. On section, it cut rather firmly. The cut surface was smooth and presented a dull, opaque, pinkish color. No focal lesions were visible.

The lymph nodes on both sides of the neck in the region of the angle of the jaw were enlarged and freely movable against one another and against the skin and deeper structures. They were discrete and rather firm in consistency. In the region of the right axilla, there was a mass immediately under the skin that was somewhat oval in outline. It was the size of a small fist, and, on cutting into it, it was found to consist of numbers of discrete lymph nodes, practically every one of which was almost completely transformed into puriform material, and the surrounding soft tissues were extensively infiltrated by pus. A similar collection of softened discrete lymph nodes was present in the left axilla. Around the pancreas were numbers of discrete nodes, varying in size from 0.5 to 1 cm. On section, they presented a swollen, edematous, cream colored or

whitish substance. The lymph nodes in the mesentery were present in considerable numbers and varied in size from 0.5 to 2.5 cm. They were discrete and, on section, swollen and edematous, some of them presenting areas of congestion alternating with whitish or cream colored patches. Enlarged lymph nodes in the pelvis were present by dozens. Some of them were discrete, swollen and edematous; many of them, however, were fused and softened to form great pockets of pus.

The right psoas magnus muscle was almost completely replaced by infiltrating tumor tissue; on section, the muscle tissue showed streaklike, pinkish areas corresponding to preserved muscular remnants, alternating with whitish or cream

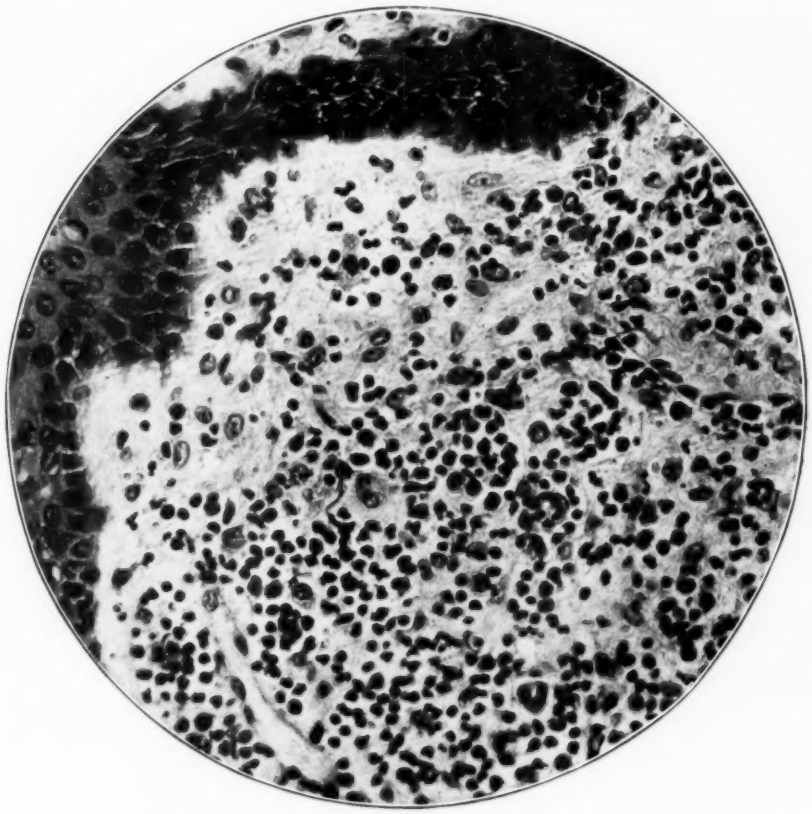

Fig. 7 (Case 2).—Section of skin from edge of an ulcerating lesion, showing tumor cells with pycknotic and crenated nuclei.

colored patches or streaks, corresponding to neoplasmic infiltration. On cutting into the right rectus abdominalis, its lower belly was found to be similarly and almost completely replaced by infiltrating tumor tissue.

The right ovary was noticeably enlarged, reaching the size of an ordinary hen's egg, and presented, on section, a diffuse dirty pinkish appearance, as if infiltrated by tumor.

The rest of the organs showed nothing of interest in the present connection, except for the presence of acute peritonitis due to the rupture of secondarily infected pelvic lymph nodes.

Histologic Examination.—Microscopic examination showed the presence of a new growth, the prevailing cell in which was slightly larger than a small lymphocyte and in which both the nucleus and the cytoplasm were less distinctly defined and the nucleus itself less richly chromatic. In some of the sections this type of cell was associated with small numbers of cells which were noticeably larger than the small lymphocyte. Wherever present, the tumor cells showed a tendency to arrange themselves in rows, bounded by strands of connective tissue.

Fig. 8.—Section from psoas magnus muscle showing tumor cells infiltrating between the muscle fibers causing pressure atrophy. Cells vary a great deal in size.

In places the rows tended to pursue a straight direction, in other places they were intercommunicating, and in still other places they were arranged circularly.

In sections from the skin, the smaller type of cell occurred exclusively, and cells of the larger lymphocytic variety were not encountered. In the spleen, however, the tumor cells practically replaced the lymphoid follicles, and in this particular organ cells of the larger variety were encountered frequently. There were moderate numbers of tumor cells of both varieties in the venous sinuses.

In the lymph nodes, the body of the node was diffusely replaced, largely by cells of the smaller type, but with a sprinkling of the large mononuclear variety. In many of the lymph nodes the capsule was richly infiltrated by tumor cells arranged in parallel lines, and in the body of the node the cells were grouped in streaks or islands, separated by delicate strands of connective tissue. The ovary was richly infiltrated by small round cells, among which were numbers of the larger mononuclear variety, the cells being arranged in parallel, intercommunicating or circular rows, each row containing, as a rule, no more than a single line of cells. Similar changes were found in microscopic sections of the infiltrated muscle tissues. Here the muscle fibers were extensively separated and compressed by tumor cells of both the large and small variety, the cells again being arranged in rows (Fig. 8).

COMMENT

We have for consideration here three cases, two of which ran a course corresponding to the clinical picture of mycosis fungoides, while the pathologic alterations in the tissues were those which are usually described as lymphosarcoma. The third was the case of a South American red squirrel that was identical, both from the clinical and pathologic point of view, with Sternberg's leukosarcoma. Comparative microscopic study was carried out on material from all of these cases. The histopathologic picture was practically the same (Figs. 1, 2, 7, and 8). There were some differences, but these were mostly referable to histologic detail, such as the size of the cells and the amount and arrangement of the chromatin content of the nuclei. The histologic picture in all was dominated by the presence of pathologic cells, round or spheroid in shape, and somewhat larger than normal lymphocytes. They were not of the small round lymphosarcoma cell type. From a morphologic standpoint they resembled the type of cell which dominates the picture in the lesion depicted by Ewing [11] as reticulum cell lymphosarcoma. The squirrel lesions occurring in lymph nodes may well be placed in this group. But what shall be said of the skin lesions with an identical histologic picture? While there is no available proof concerning the origin of these lesions, the suggestion is offered on morphologic grounds that they arise from the reticulo-endothelial cells of the skin that exist in great numbers in the perivascular tissue in the upper portions of the corium. Confirmation of this view would necessitate designating the lesion in mycosis fungoides as a "reticulum cell sarcoma." The two human cases here recorded, together with three cases of mycosis fungoides that I recently reported,[12] make a total of five cases of this disease, in all of which the pathologic changes in the tissues were unquestionably neoplastic. These

11. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, p. 382, 1922.

12. Fraser, J. Frank: The Interpretation of Mycosis Fungoides as a Variety of Lymphosarcoma, Arch. Dermat. & Syph. **2**:425-445 (April) 1925.

cases do not stand alone. Within a period of one year, Keim [13] has encountered three cases of clinically typical mycosis fungoides which were followed by necropsy. In all of his cases the pathologic findings were those of lymphosarcoma. In one of the cases the neoplasm infiltrated the kidneys, pancreas, testes and gastro-intestinal tract.

The question of whether the lesion in mycosis fungoides is inflammatory or neoplastic again faces us. In the present series and in Keim's cases the lesions were unquestionably neoplastic. Are the lesions in mycosis fungoides always neoplastic, or are they always inflammatory as practically every textbook would have us believe? Or are the lesions inflammatory in the early stage of the disease and later transformed into a neoplastic process? In a recent article,[12] I analyzed these questions and concluded that the lesions were neoplastic from the beginning. The inflammatory features which often dominate the histologic picture, especially in the early or prefungoid dermatoses, were interpreted as a reaction to the development of tumor cells.

As to the relation of mycosis fungoides to leukemia and other lymphoid hyperplasias,[13] Keim expresses the belief that leukemia, mycosis fungoides, lymphosarcoma and Hodgkin's disease are genetically related. Symmers [14] points out that "chronic lymphatic leukemia and its companion lesion, pseudo-leukemia, together with the various types of lymphosarcoma, present many clinical and anatomic changes in common. Not only are the histologic alterations closely akin, but, in many instances, they are indistinguishable one from the other." He places Hodgkin's disease, however, in a category by itself, at the same time emphasizing the belief that there are certain cases of mycosis fungoides in which the histologic changes are similar to those of Hodgkin's disease. Mallory [15] regards the lesion in Hodgkin's disease as a scirrhous form of lymphosarcoma, and lymphatic leukemia as a lymphosarcoma growing in the circulating blood. Lenarz [16] also considers lymphatic leukemia as a neoplastic process.

SUMMARY

Two cases are added to the growing number of instances of mycosis fungoides in which the pathologic changes in the tissues are unquestionably neoplastic.

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13. Keim, Harther L.: Universal Leukemia Cutis, Arch. Dermat. & Syph. **10**:579-598 (Nov.) 1924.

14. Symmers, Douglas: Certain Unusual Lesions of the Lymphatic Apparatus, Arch. Int. Med. **21**:237 (Feb.) 1918.

15. Mallory: Principles of Pathologic Histology, Philadelphia, W. B. Saunders Company, pp. 326-332.

16. Lenarz, L.: Il concetto della leucemia, Haematologica **3**:173, 1922.

Evidence is presented which shows a genetic relation between mycosis fungoides, lymphatic leukemia and lymphosarcoma.

The name reticulum cell sarcoma is suggested to replace the term lymphosarcoma in designating the lesion of mycosis fungoides. The suggestion is based on the assumption that the lesion has its origin in the reticulum cells of the papillary layer (reticulo-endothelial system of the skin).

21 West 54th Street.

DISCUSSION

DR. WALTER J. HIGHMAN, New York City: I have been much interested in the subject of Dr. Fraser's paper and a great deal of what I have in mind I was able to relieve myself of two or three weeks ago, at greater length, in Washington. I think the facts which Dr. Fraser has propounded are difficult to prove until we have more knowledge of the interrelationship of the various diseases. I think Dr. Weidman touched on this in Washington when he said that until we have more knowledge of the connection of the entire group we are all talking at random. I am personally of the belief that Dr. Fraser is correct, but how the fact is to be established I do not know, and I think Dr. Fraser does not either.

As to the definition of terms, we talk of granuloma fungoides and lymphosarcomatosis as it regards the skin, and the other related conditions, really not knowing what we are talking about, and yet we use the different terms. Dr. Fraser has just reported five cases in which clinically the patient seemed to be suffering from mycosis fungoides, but in the laboratory this was not found to be the case. What do we mean when we say mycosis fungoides if it clinically looks like mycosis but pathologically is something else? I think to clarify the terms it would be well to do something along the line of a scheme I would like to mention. Mycosis fungoides, lymphosarcomatosis and Hodgkin's disease do look alike. Why not confine our conception of mycosis fungoides to that group in which we can prove it, and that means by examination of the skin? If we do not find these particular characteristic features the first time we make a histologic study, perhaps we will the second or third time.

Second, in talking of leukemia cutis, why do we not confine our conception of that term to that disease which clinically looks like any of the four diseases but studied pathologically is found to be leukemia?

Why do we not confine our conception of Hodgkin's disease to that which occurs in the glands, and why do we not confine our conception of lymphosarcoma to that which looks like lymphosarcoma histologically in the cutaneous sections as well as in other tissues in vivo? I say in vivo because being right, as proved after death, is of little value to the patient.

This seems arbitrary, perhaps childish, but if we do have this in mind after we study more in the laboratory, the hypothetical toxic agents which may cause any or all of these lesions, we will at least know when discussing this subject that we have some point of departure. I do not offer this as anything final but as a tentative scheme for clarifying our terms. It is not possible indefinitely to cut out lymph glands of the patients who look as if they had Hodgkin's disease, but if the blood count never shows leukemia and the skin picture is not that of mycosis, it is fair to assume that we are dealing with Hodgkin's disease, and so on down the line. This is the suggestion I wish to submit. I think it has nothing of the hysterical in it, and it may have a few of the advantages of common sense.

Dr. Udo J. Wile, Ann Arbor, Mich.: In connection with the department of pathology, we have studied some dozen or more cases of so-called mycosis fungoides which have come to a postmortem examination. We have found a great variation in the gross, as well as the microscopic pathology of the cases, even when they were clinically identical. For example, in one typical case, the tumors were found to be made up almost entirely of eosinophils, several others presented the gross and microscopic pathology of lymphosarcoma or of round cell sarcoma, and in still a third group the microscopic picture was that usually thought to be associated with mycosis fungoides, that is, of cells of different types. We have come to the belief that it is better to regard mycosis fungoides as a clinical variety of what might properly be called malignant lymphoblastoma. This classification would link the condition up with leukemias with cutaneous manifestation on the one hand and with true lymphosarcoma on the other.

I cannot subscribe to Dr. Highman's suggestion that the term mycosis fungoides should be applied only to cases in which the microscopic picture is typical; first, because I do not believe that there is a typical picture, and second, because long usage in teaching has established mycosis fungoides as a clinical entity at least, irrespective of its pathologic picture.

The long prodromal stage of a more or less innocent dermatitis followed by typical infiltration and more typical ulcerative tumors constitutes so striking a clinical entity that it should not be given up as such.

To meet the issue squarely, one can regard these cases as pathologically lymphoblastomas of the mycosis fungoides type.

Dr. Hermann Feit, Jersey City, N. J.: Whether mycosis fungoides is a neoplastic or inflammatory tumor is not yet settled. However, I would like to say a few words about treatment.

I have a patient who has been affected with skin disease for twenty-five years. It began as psoriasis, which developed into so-called "exfoliative dermatitis," and which is now mycosis fungoides. She had been treated with the roentgen ray for many years, and she is at present covered with roentgen-ray burns. Under the treatment to be described this patient, who suffered for so many years with intense itching, is undergoing great improvement.

The treatment consists of intravenous injections of neo-arsphenamin dissolved in a ureate of calcium. The ureate of calcium prevents the untoward effects of the arsphenamin because of its calcium content, and it also relieves the itching. Following the injection of the ureate of calcium the patient is flushed, has a feeling of warmth, and sometimes there is perspiration.

The patient in question is in the infiltrated stage of the disease and biopsy shows all the features of mycosis fungoides.

The combination of arsphenamin with the ureate of calcium seems to be an improvement in the treatment of mycosis fungoides.

Dr. J. Frank Fraser: I wish to say that the many identical histologic pictures of this disease are too frequent to be regarded as accidental. Recently I have been in the habit of interpreting histologic pictures, not only in mycosis fungoides but in other diseases, in the light of their clinical behavior. I consider this comparison highly desirable. If we have a slide showing the early changes, the multiformity of cells that we find and the perfectly typical clinical picture of mycosis fungoides, I think we are justified in making that diagnosis. I base my theory as to the origin of the cells on their morphologic characteristics. Dr. Wile suggested their origin from primitive lymph nodes in the skin. I have talked this over with several histologists, and they deny that primitive lymph nodes ever exist in normal skin. However, for the present I think it best to leave the question unsettled.

MICROSCOPIC CONDITION OF SPINAL CORD IN PEMPHIGUS

REPORT OF A CASE

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It is evident that lesions of the spinal cord in pemphigus are not a constant finding. Covey [1] reports lesions similar to those herein reported. Kraus [2] reports two cases showing no pathologic changes in the nerve cells, connective tissue cells, blood vessels, roots or meninges in the sections examined, at the cervical, thoracic and lumbar levels.

REPORT OF CASE

History.—J. S., a Mexican woman, aged 47, was admitted to Robert B. Green Memorial Hospital, San Antonio, Oct. 1, 1924, and died that night. Her weight was apparently 180 pounds (81.6 kg.). The history was difficult to obtain, but this appeared to be the third attack of a similar character. She had enormous bullae over the hips and abdomen and between the shoulders, and many small ones in various stages of involution over the trunk and extremities. Many healed lesions suggested that the disease was chronic.

Necropsy (Dr. W. H. Hill).—The general appearance was that of a middle-aged Mexican woman with generalized edema, especially marked about the eyelids, feet and ankles. The skin showed a rather generalized eruption in the form of vesicles and bullae, some clear, some pustular, but most of them hemorrhagic. The superficial epidermis was gone from the right buttock, probably due to rupture of large bullae. The vesicles and bullae were more numerous over the buttocks, breast, legs and ankles. There were many old scars over the body from old lesions, some of these looking older than the duration of illness—one month. Blood was oozing from the mouth and there were blood clots around old tooth snags and gums.

The brain and spinal cord showed no pathology macroscopically. The heart was greatly hypertrophied—it was two or three times its normal size. Ventricular hypertrophy was more marked on the left than on the right. The chambers of the heart were dilated, especially the left auricle. The mitral valves showed marked arteriosclerosis, with narrowing of the opening. The aortic valves also showed some thickening, with one or two small vegetations. The aorta, lungs and spleen were normal. The liver was moderately enlarged, showing a nutmeg appear-

1. Covey, G. W.: Pemphigus Vulgaris with Findings in the Spinal Cord Suggesting the Etiology of the Skin Lesions: Report of a Case, Arch. Dermat. & Syph. **9**:305, 1924.

2. Kraus, W. M.: Postmortem Findings in the Spinal Cord in Two Cases of Chronic Pemphigus, Arch. Dermat. & Syph. **10**:424, 1924.

ance on section and passive congestion. Both kidneys were small, showing chronic nephritis, the capsule stripping with difficulty. The bladder contained a small amount of bloody urine. The uterus, tubes and ovaries were atrophic. The intestines and stomach were normal. The cause of death was toxemia from pemphigus.

Neurologic Report (Dr. William Keiller).—The spinal cord showed no gross pathologic lesions.

Microscopic Report.—Cervical Enlargement: A low power magnification and hematoxylin-eosin stain showed small hemorrhages scattered through the cord, with no apparent prevalence in distribution. Corpora amylacea were prevalent

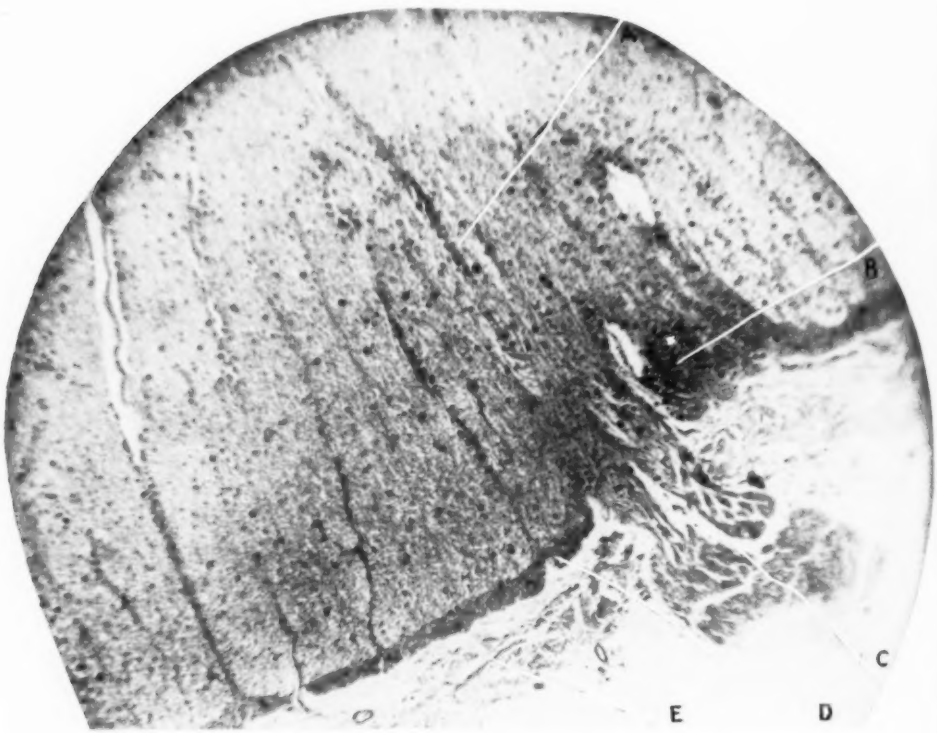

Fig. 1.—Cervical enlargement, showing corpora amylacea of general distribution, but most abundant in the posterolateral (Lissauer's) column, neuroglial septums and in subpial neuroglia. *A* indicates a neuroglial septum; *B*, the posterolateral column (Lissauer's); *C*, the posterior nerve root; *D*, the subpial neuroglia; *E*, the pia-mater. (Low power magnification.)

in great numbers everywhere, but especially in the peripheral neuroglia at the entry of the posterior nerve roots and in the posterolateral (Lissauer's) column (Fig. 1), next round the central canal (Fig. 2), then in all the glial septums and in the subpial neuroglia. They were much more numerous in the posterior white columns than elsewhere in the white substance. None get outside the neuroglia; none are in the pia, and none have been found in the posterior nerve roots outside the cord substance. They were frequently so numerous between

the entering posterior nerve roots that it seemed likely that they may have caused interference (by pressure) with the root function. They were heaped up around blood vessels in the neuroglia surrounding the perivascular sheaths.

While the corpora amylacea were very numerous at the entrance of the dorsal nerve roots, they were not especially numerous at the exits of the ventral nerve roots.

Under high power magnification, some of the ventral gray column cells were healthy, showing typical cytoplasm and central nuclei, especially those in the ventromedial group; most of the cells of the lateral column groups were degenerated, showing brownish, mostly unstained cytoplasm and excentric nuclei. A

Fig. 2.—Cervical enlargement, showing corpora amylacea in posterior column, in gray matter around the central canal and in the walls of the anterior median fissure. *A* indicates the posterior columns; *B*, the central canal; *C*, the pia-mater in the anterior median fissure. (Delafield's hematoxylin and eosin stain; low power magnification.)

small group of two or three cells in the position of the nucleus dorsalis (Clarke's column) showed degeneration.

The corpora amylacea, which at first showed marked affinity for the toluidin blue stain, bleached rapidly and completely. The nerve cells showed the same changes as in hematoxylin eosin sections.

Midthoracic Cord: The Delafield hematoxylin-eosin stain was used. Low power magnification showed a decided lack of cells in the ventral gray column

and nucleus dorsalis. At medium power magnification, the cells of the nucleus dorsalis (Clarke's column) were very few and showed marked degeneration. The intermediolateral cell column was practically absent. All nerve cells showed degeneration. The corpora amylacea were about the same in distribution but not quite as numerous as in the cervical region. The vessels showed some hyaline thickening of the inner coat. There were no hemorrhages. The central canal was absent; there was no central epithelium or a few epithelioid cells only. No distinct canal or columnar cells were present. There were decidedly fewer corpora amylacea in the subpial neuroglia.

Lower Thoracic: Hemorrhages were numerous in one anterior gray column and a few scattered hemorrhages occurred in the other gray matter and in the white columns. There was one fairly good sized hemorrhage on one side of the gray commissure.

The corpora amylacea were about the same as in the midthoracic cord. In the nucleus dorsalis there were eight or nine cells. They were all degenerated. The central canal was about the same as the midthoracic cord.

All nerve cells showed marked degeneration. The intermediolateral cell column showed only a few cells, all markedly degenerated.

About the same results were obtained with the toluidin blue stain.

Lumbar Enlargement: With a low power magnification and the hematoxylin-eosin stain very few and small hemorrhages were shown. The corpora amylacea were about as numerous as in the lower thoracic region. Where the posterior root was breaking through the neuroglia, the corpora amylacea passed out in the root until it penetrated the neuroglia, not farther. There were none in the posterior roots. They were most numerous just lateral to the entrance of the posterior nerve roots. The vessels showed no thickening of their walls.

With a high power magnification one or two corpora amylacea were seen in one posterior nerve root before it entered the cord. All nerve cells showed marked degeneration.

Posterior Root Ganglia.—One ganglion in each region was examined. In the cervical region, with low power magnification, many of the ganglion cells showed a finely granular brown pigmentation, and in most the cytoplasm stained poorly and no nuclei were visible. There were no hemorrhages, and there was no round cell infiltration.

In the midthoracic region, with a toluidin blue stain, there were areas in the cytoplasm which had almost completely failed to take the stain. There was also pigmentation of the cytoplasm. There was no necessary correspondence between the presence of pigmentation and the failure of the cytoplasm to stain, pigmentation sometimes being found in the midst of well stained cytoplasm, or cells with large areas of poor staining showing no pigment. The pigment was brown and finely granular, and differed from the black, coarsely granular pigment frequently found in anterior gray column cells of aged subjects. Results with the hematoxylin-eosin stain were the same as in the cervical region.

In the lower thoracic region the results with the hematoxylin-eosin stain were the same as in the cervical and midthoracic regions.

The lumbar region was the same as the others, but there appeared to be some relation between the loss of staining properties and pigmentation, the one condition appearing to merge into the other. No hemorrhages into the ganglia were observed, except in the section from the midthoracic region stained with hematoxylin-eosin in which there was a hemorrhage which appeared to be accidental. No pathologic alterations were observed in vessel walls in any of the ganglia.

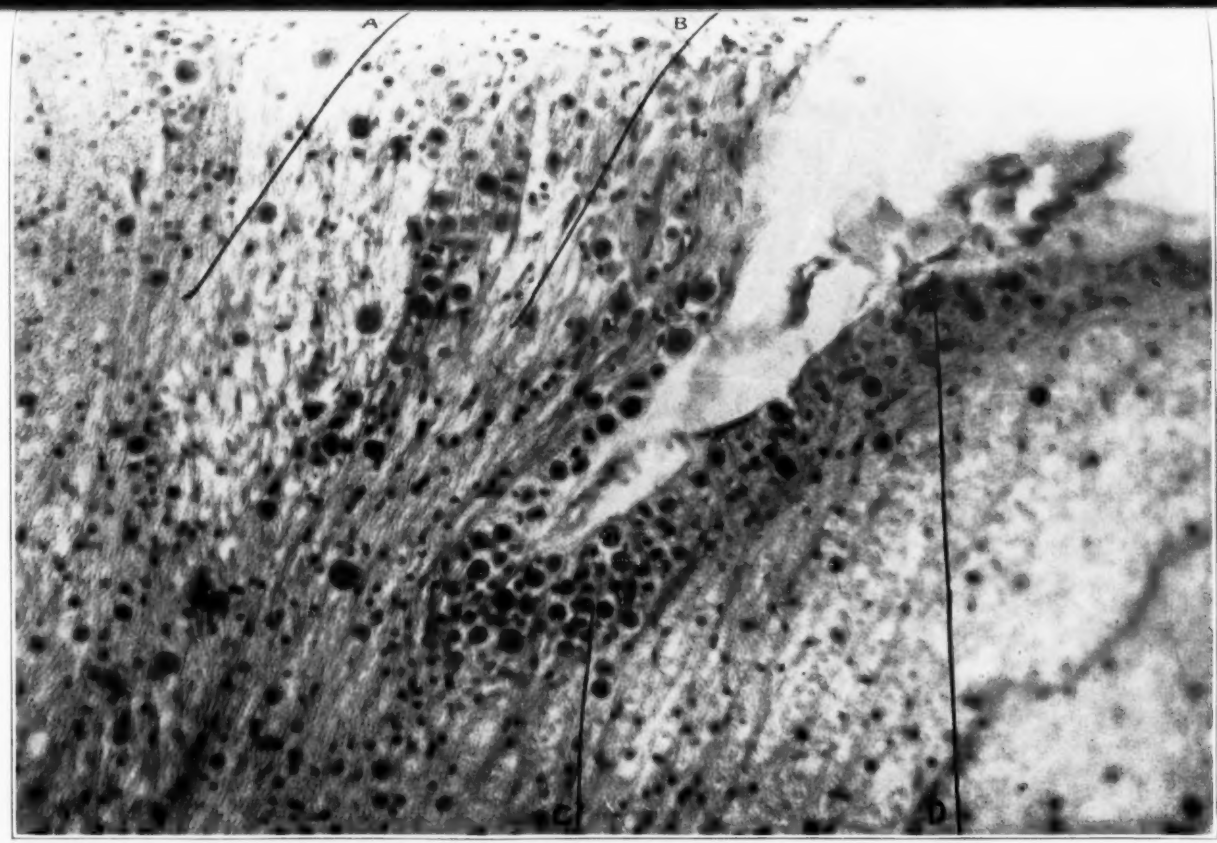

Fig. 3.—Cervical enlargement, showing entrance of posterior nerve root. This is a typical high-power magnification picture of corpora amylacea as stained by Delafield's hematoxylin. Their varying size, the diffuse purplish blue stain with hematoxylin and their distribution, the dark center shading off toward the periphery, the absence of cell structure and an appearance of concentric lamination are typical. *A* indicates the posterior column; *B*, fibers of the entering nerve root; *C*, corpora amylacea in the subpial neuroglia superficial to the posterolateral (Lissauer's) column; *D*, subpial neuroglia with corpora amylacea.

In a section through the middle of the inferior olive with low power magnification and hematoxylin-eosin stain, corpora amylacea were seen scattered everywhere. They were abundant in the subpial neuroglia, especially along the ventral surface. They were numerous in the superficial neuroglia of the floor of the fourth ventricle. They were also numerous in almost all the septums of the neuroglia passing in from the surface. A few were found among the fibers of the medial lemniscus. They were numerous in the spinal tract of the fifth nerve and in the pial tissue surrounding blood vessels. The cells of the hypoglossal nucleus appeared to be normal, showing little or no degeneration.

The cells of the nucleus lateralis were almost normal; so also were the cells of the superior olive. All the blood vessels were normal, and in these there was

Fig. 4.—Lower thoracic cord, showing vessels full of blood and many small hemorrhages, especially in anterior gray column. The erythrocytes are stained nearly black. (Iron hematoxylin [Heidenhaim] paraffin section; alum carmine counter-stain.) *A* indicates the central canal; *B*, the anterior median fissure; *C*, hemorrhage near the central canal; *D*, hemorrhages in the anterior gray column.

no suggestion of syphilis. A little lower in the oblongata, before the central canal opened out into the fourth ventricle, the corpora amylacea were abundant in the subpial neuroglia, all round the oblongata and where the pia mater dips into the anterior median fissure. They were also abundant around the central canal, just as they were around the central canal of the spinal cord. Wherever neuroglial septums dipped in from the surface, especially in the anterior pyramids, the corpora amylacea were packed closely in the septums. They were also abundant in the

neuroglia surrounding blood vessels. There were no hemorrhages, and the nerve cells showed central nuclei which stained fairly well.

There were occasional corpora amylacea in the white matter of the cerebellar hemispheres. There were no vascular changes, but there were occasional minute hemorrhages.

In the superior vermis were many corpora amylacea in the white center; the blood seemed always to be within capillary walls. There were no hemorrhages. No other changes were observed. The vessels were normal.

Summary.—By far the most striking feature was the enormous number of corpora amylacea. While numerous everywhere, these were especially marked in the posterior columns (Fig. 1), in the subpial neuroglia (Fig. 3) and in the glial septums which stretched inward from the surface, as well as in the posterolateral column (Fig. 1) and around the central canal (Fig. 2).

Capillary hemorrhages were the second most striking feature, especially in the section of the lower thoracic cord (Fig. 4).

The third feature was the apparent disappearance of many of the anterior horn cells and cells of the nucleus dorsalis and marked degeneration of those that remained.

Myelin stains showed no tract degenerations. Posterior root ganglions showed pigmentation and chromatolysis of the nerve cells, but no hemorrhages.

COMMENT

Buzzard and Greenfield, in their "Pathology of the Nervous System," 1921, under the head of "Corpora Amylacea," state: "They are normally found in the cords of elderly persons, being most common around the periphery of the cord, but present in both grey and white matter. They stain diffusely blue with hematoxylin stains, especially Weigert's Iron Hematoxylin. They appear to be derived from neuroglia as they may be found in gliamota, but their mode of origin is unknown. They have no pathological significance."

We have found corpora amylacea widely distributed in sections of spinal cords, and one of our series belonging to a case diagnosed as taboparesis, and showing distinct evidence of meningeal syphilis (lymphocytic infiltration of the pia-mater), showed them in great abundance. In the same case of taboparesis there were a few corpora amylacea in one of the posterior nerve roots, a considerable distance from the spinal cord.

Other cords with similar lymphocytic infiltration of the pia-mater showed corpora amylacea rather numerously, but in no case were they so numerous as in the pemphigus cord under discussion. A pellagra cord showing marked degeneration has only a few corpora amylacea.

The nerve cell degenerations are not more marked than one usually finds in cords of patients dying of profound infections. We have found no other cord, except in traumatic cases, which showed such hemorrhages as those illustrated in Figure 4. It is believed, however, that all the lesions found in the cord are the result of profound toxemia and are in no way accountable for the skin lesions.

CONTRADICTORY FINDINGS BY DR. W. KEILLER

The foregoing case appears to indicate that the great number of corpora amylacea is the most characteristic finding in the brain stem and cord in patients dying of pemphigus. However, almost immediately after the case reported above, I had the privilege of examining the brain and cord in a second patient with pemphigus who died in the John Sealy Hospital, Galveston, Tex. In this case, which will be reported fully, greatly to my surprise, there were no corpora amylacea and degeneration of the nerve cells, and occasional microscopic hemorrhages were the only pathologic lesions common to both cords.

Besides the neurologic findings, the chief difference between the two cases was that the case reported above was that of an exceedingly fat woman, while in the case to be reported later the patient was extremely emaciated. Possibly the extreme emaciation and presumably carbohydrate hunger might account for the absence of corpora amylacea.

FUSIFORM BACILLI AND SPIROCHETES

XII. OCCURRENCE IN GANGRENOUS LESIONS OF FINGERS: REPORT OF A CASE *

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In previous studies,[1] it was pointed out that putrid infections were often caused by fusiform bacilli and spirochetes, and their source was related to the distribution of these bacteria on the human body. A rare and striking lesion is the gangrenous infection of the finger resulting from injury inflicted by teeth about which these anaerobes are found normally. Hultgen [2] reported such a lesion containing these organisms in a girl, aged 7, who had the habit of biting her finger nails. Peters [3] described two instances as a result of fists striking teeth. The first man injured his index and middle finger, where foul, discharging ulcers formed. In these lesions fusiform bacilli and streptococci but no spirochetes were demonstrated. In the second, the foul pus discharged from the left little finger from an irregular, ragged ulcer for eighteen days. The bacilli and spirochetes were observed first and later a few cocci and small bacilli appeared. The ulcer did not heal until fifty-four days after injury.

REPORT OF CASE

Our patient, E. M., aged 28, colored, presented a more destructive lesion of the middle finger of the left hand of three weeks' duration. In a fight, his finger was bitten and became swollen the next day. A week later, the swelling on the radial side of the terminal phalanx was incised. Subsequently, the lesion became deeper and discharged foul pus. Hot moist dressings were applied.

On examination the patient appeared normal except for the lesion on the middle finger of the left hand (Fig. 1). The ulcer was deep, beginning from the base and sides of the distal phalanx, involving the entire circumference of the middle and extending to the dorsal surface of the proximal phalanx. The lesion was moist and dark green; the base presented bony tissue in the center and a black irregular slough around the bone. The margins were irregular, shaggy, and bled readily. The discharge consisted of a thick, blood-tinged, purulent material with a putrid odor. The epitrochlear and axillary glands were not

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1. Davis, D. J., and Pilot, Isadore: Studies of Bacillus Fusiformis and Vincent's Spirochetes. I, J. A. M. A. **79**:944 (Sept. 16) 1922.

2. Hultgen, I. J.: Partial Gangrene of Left Index Finger, J. A. M. A. **55**:857 (Sept. 3) 1910.

3. Peters, W. H.: Hand Infections Apparently Due to Bacillus Fusiformis, J. Infect. Dis. **8**:455 (June) 1911.

enlarged or tender. The temperature varied from 98 F. to 99 F.; the pulse rate was from 80 to 90. The Wassermann reaction on the blood was negative. On the roentgenogram of the finger the middle phalanx presented an interruption of continuity with a ragged periosteum. The interpretation of the roentgenologist was an old fracture with superimposed infection or a deep, destructive infection.

Smears of the pus revealed many fusiform bacilli, spirochetes and few streptococci and diphtheriods. On the basis of bacteriologic findings, two doses of 0.6 gm. of neo-arsphenamin were administered intravenously. As the distal phalanx was hanging loosely supported by strands of soft tissue, it was decided to amputate. The middle phalanx was divided. The proximal end was a green, granulating surface; the distal portion consisted of black, necrotic tissue. Two doses

Fig. 1.—Gangrene of middle finger.

of 0.6 gm. of neo-arsphenamin were given subsequently. The ulcer rapidly diminished in size, and was entirely healed eight days after amputation.

Smears of the pus were stained with 10 per cent. carbol-fuchsin and by the Fontana method. The fusiform bacilli varied from 4 to 15 microns in length, occurring as straight or curved rods, either solid or granular. Thread forms were numerous (Fig. 2). The spirochetes appeared as short or long, fine or coarse spirals of from 3 to 8 turns. In their morphology these bacteria appeared identical with those observed about normal and diseased teeth and tonsils and in putrid infections of the lungs.[1] Aerobic cultures on blood agar plates revealed *Streptococcus hemolyticus* and diphtheroids. In anaerobic blood agar slants similar organisms, together with pleomorphic forms of *Bacillus fusiformis*, appeared.

Microscopic examination of sections from the amputated finger presented granulation tissue made up of loose connective tissue and young vessels covered by a necrotic layer. The deeper tissues were densely infiltrated, chiefly with plasma cells, lymphocytes and many eosinophils. Few polymorphonuclear leuko-

cytes were seen. In the necrotic surface layer, numerous degenerated leukocytes, tissue débris and bacteria occurred. In Levaditi preparations, bacilli and cocci, but no spirochetes, were seen. However, the absence of spirochetes may be explained by the neo-arsphenamin therapy before amputation.

These lesions of the fingers are of great interest because they illustrate the pathogenicity of the anaerobes formed in the discharge. Indeed such an infection following trauma from teeth, where these bacteria thrive in large numbers, can be compared to a lesion that is

Fig. 2.—Fusiform bacilli, spirochetes and cocci in smear from gangrenous lesion of middle finger (Fontana stain).

experimentally produced. The destructive character, the putridity of the ulcer and the response to neo-arsphenamin is similar to that observed in lesions associated with fusiform bacilli and spirochetes in ulcerative stomatitis, gangrenous balanitis and pulmonary abscess and gangrene.[4]

In all the anaerobic infection is complicated by the presence of certain pyogenic bacteria, particularly streptococci.

4. Pilot, Isadore, and Davis, D. J.: Studies in Fusiform Bacilli and Spirochetes. IX. Their Role in Pulmonary Abscess, Gangrene and Bronchiectasis, Arch. Int. Med. **34**:313 (Sept.) 1924.

HYPERCHOLESTEROLEMIA

II. THE EXPERIMENTAL INDUCTION OF HYPERCHOLESTEROLEMIA *

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AND
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When a condition like hypercholesterolemia bears an important relation to different human diseases, its experimental production in animals must appeal as one of the first implements to acquire when experimentally investigating such disease states. To do this qualitatively is not difficult—cholesterol cramming suffices. But such data as the amounts necessary to be fed, and, once induced, the quantitative variations in different animal species, the speed of development, duration, intensity, i. e., refinements of hypercholesterolemia, do not appear to have been collected. Probably this would have been done long ago had the quantitative chemical technic been more satisfactory. The situation may be gathered from our preceding communication.[1]

The last disconcerting blow was a personal communication from Luden to the effect that the anticlotting substances, sodium citrate and calcium oxalate, produce fluctuations of the cholesterol figures "in a wholly irregular way." If Luden's point is well taken, the whole fabric of cholesterol analysis will be disarranged. This much, however, is certain, that as cholesterol technic stands today, the only reliable data are the comparative; i. e., when the worker, using the same technic throughout, has established normal figures on a sufficiency of normal controls before essaying conclusions.

THEORETICAL AVENUES FOR INTRODUCING CHOLESTEROL

1. Feeding by mouth.
2. Introduction by stomach tube.
3. Introduction by rectum.
4. Injected interstitially (subcutaneously or intramuscularly).
5. Injected intrathecally (peritoneum, pleura, etc.).
6. Injected intravenously.
7. Induction of basal metabolic upsets with drugs or otherwise.

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1. Weidman, Fred. D., and Sunderman, F. William: Studies in Hypercholesterolemia. I. The Normal Blood Cholesterol Figures for Man and the Lower Animals, Arch. Dermat. & Syph. **12**:679 (Nov.) 1925.

Certain ones of the foregoing methods are impracticable in dealing with experimental animals. Thus, rectal feeding would be pretty sure to fail on account of more or less prompt expulsion. Of the intrathecal injections, only the peritoneal route appeals—operative difficulties do not bulk as large. The stomach tube is unnecessary except in quantitative work, because cholesterol is in a form readily enough and more easily administered by feeding. The last method cited is no more than conceivable at present, although some workers have broached it. Thus Palacio [2] excised the suprarenal cortices of rats, and found that the blood serum cholesterol was not decreased in consequence. He believes that the cortex serves as a reservoir or as a chemical transformer of cholesterol rather than as a specific secretory organ. While on this subject, it might be noted in passing that Leupold and Seisser [3] observed local cholesterol deposits in the ovaries of cats following extirpation of suprarenals, and that after removing one suprarenal there was a reduction of blood cholesterol which was restored only after some time. They also showed that thyroid feeding and the administration of diphtheria toxin induced a reduction of from 23.5 to 35.6 mg. per hundred cubic centimeters in rabbits' serum.

The remaining methods of cholesterol introduction have been used by one or more workers, and will be covered separately hereafter. Wacker and Hueck [4] remind us that in all these the proper respect must be paid to conditions of work, breathing, restraint and nourishment.

In our survey of the literature (the literature on cholesterol is enormous), we found reports frequently enough of the feeding and injection of cholesterol, which were directed at questions other than the induction of hypercholesterolemia, i. e., to such problems as absorption from solid tissues, routes of elimination, induction of atheroma, etc., and in connection with which no blood cholesterol determinations, such as would be useful to us, were made. After eliminating these, a very small number of reports, indeed, remained for our purposes. In the latter it stood out clearly that hypercholesterolemia has been induced mostly by the oral route.

FEEDING BY MOUTH

The substances employed were: chemically pure cholesterol, more or less crude cholesterol (extractives of gallstones) and foods rich in cholesterol, such as egg-yolk, brain tissue, etc. On account of the irregularities of absorption rate and volume, no fixed dosage appears to have been attempted, and these irregularities also render this method unsuitable for most quantitative work.

2. Palacio, J.: Prensa med. Argentina **9**:1014, 1923.
3. Leupold, E., and Seisser, Franz: Arch. f. Gynäk. **119**:552, 1923.
4. Wacker, L., and Hueck, W.: Arch. exper. Path. u. Pharmakol. **74**:416, 1923.

The first outstanding experiments involving mouth feeding were those of Pribram,[5] although cholesterol had previously been fed by several investigators. In 1906, he administered, through a stomach tube, cholesterol, cholesterol oleate and cholesterol palmitate in an olive oil emulsion to rabbits for three successive days. Analyzing the total blood in the animal's body, it appears from his tables that he obtained as much as from 50 to 600 per cent. increase in the cholesterol content!

In 1907, Morgenroth and Reicher[6] fed a rabbit with cholesterol. One control received olive oil and a second one an ordinary diet. The blood of the cholesterolized rabbit yielded 480 mg. per hundred cubic centimeters of blood, and the control 30 and 26 mg., respectively. This is a most remarkable increase, especially in view of the extremely low figures of the control animals. These are comparative values, and must be accepted because the same technic was used in all the determinations.

In 1909, Doré and Gardner[7] obtained a blood cholesterol figure of 415 mg. per hundred cubic centimeters in a rabbit which had been fed for ten days on bran fortified with 2.25 gm. of cholesterol. Controls which had been fed decholesterolized bran showed little more than a trace of cholesterol in the blood. In six rabbits with normal diets the cholesterol figures averaged 24 mg. per hundred cubic centimeters of blood. Fraser and Gardner confirmed this work the next year, using the Windaus digitonin technic.[8]

Lehmann[9] has given us information as to the immediate effects of cholesterol feeding in respect to the rate of absorption. Following a cholesterol cramming through the use of the stomach tube in rabbits there was an initial fall in the blood cholesterol for from six to eight hours, ascribable, he thinks, to the hemorrhages incident to the frequently repeated blood examinations. At the end of twenty-four hours, the blood figure was at its height, the cholesterol increase being 20 per cent. above normal. After this there was a gradual fall throughout the next two days.

By feeding cholesterol to rabbits, Wacker and Hueck[4] found that the amount of cholesterol in the blood was increased (on the basis of a normal figure of 92 mg. per hundred cubic centimeters). They induced a hypercholesterolemia varying from 158 to 357 mg. To do this it was necessary to feed from 90 to 231 gm. of cholesterol over a period varying from thirty-seven to 203 days.

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5. Pribram, H.: Biochem. Ztschr. **1**:414, 1906.
6. Morgenroth, J., and Reicher, E.: Berl. klin. Wchnschr. **44**:1200, 1907.
7. Doré, C., and Gardner, J. A.: Proc. Roy Soc. London **81**:109, 1909.
8. Fraser, M. T., and Gardner, J. A.: Proc. Roy. Soc. London **82**:559, 1910.
9. Lehmann, E. P.: J. Biol. Chem. **16**:495, 1913.

Grigaut and L'Huillier [10] obtained an increased blood figure in two dogs by addition of cholesterol to ordinary diet. One dog received 1 gm. and the second 2 gm. daily. Expressing the cholesterol in terms of total quantity in the circulating blood, and with a normal of 2 gm. there was an average increase of 50 per cent. in the first dog and 75 per cent. in the second. This persisted as long as feedings were maintained. The hypercholesterolemia dropped to normal within three days after discontinuing cholesterol feedings (only the second dog was tested in this respect). This confirms the experience of Pribram that the hypercholesterolemia induced by an oral feeding was transient.

Gardner and Lander [10a] studied the effects of diet and starvation on the cholesterol contents of the various tissues of cats; their results may also have a value in connection with normal figures. They used the Fraser and Gardner modification of Windaus' method.

The findings for blood are given in the table.

Effects of Diet and Starvation on Cholesterol Contents of Tissues of Cats

	Cat	Cholesterol	Cholesterol Esters	Total Cholesterol and Cholesterol Esters
Cholesterol—poor diet (egg white and potato)..	1	44	0	44
	2	46	14	60
	3	56	02	58
	4	40	04	44
Meat diet	1	66	17	83
	2	54	24	78
Starvation	1	74	89	163
	2	69	127	196
	3	126	25	151

It seems to be established that fat cannot be substituted for cholesterol if we would be certain of producing a hypercholesterolemia, for whereas Terroine [11] reported that he was able to do so by feeding fats to dogs, Bloor,[12] analyzing blood at intervals over a period of eight hours, found only small and irregular variations in the cholesterol content.

We may accept Rothchild's [13] figures for rabbits. By feeding 0.4 gm. of cholesterol daily, the normal figure was doubled in about seven days; in twenty-eight days it had reached two and one-half times the normal; and in forty days, it was six times the normal. By feeding 0.3 gm. of cholesterol in capsules to goats, Luden [14] noted an increase of 90 and 62 gm. in the blood cholesterol figure (normal, 170).

10. Grigaut, A., and L'Huillier, E.: Compt. rend. Soc. de biol. **73**:304, 1912.
10a. Gardner, J. A., and Lander, P. E.: Bio-Chem. J. **7**:576, 1913.
11. Terroine, E. F.: J. Phys. Path. Gen. **16**:386, 1914.
12. Bloor, W. R.: J. Biol. Chem. **23**:317, 1915.
13. Rothschild, M. A.: Beitr. z. path. Anat. u. z. allg. Path. **60**:39, 1915.
14. Luden, G.: J. Biol. Chem. **27**:273, 1916.

In testing the therapeutic effect of cholesterol on experimental tuberculosis of rabbits, Jaffe and Levinson [14a] fed cottonseed oil plus cholesterol to some rabbits, and egg yolk to others. They reported the normal figure for rabbits (Bloar technic) as from 80 to 90 mg. After two months' feeding of the cholesterol-oil mixture, the figure rose to 250 mg., and after five months to 833 mg. On egg yolk the increase was not so great, but was still remarkable—330 mg. after two months, and 508 mg. after five months, i. e., a nine or tenfold increase. This is the most extreme increase which has been definitely shown by any method.

We find only one record in which the white mouse was concerned. Leupold and Bogendorfer [15] increased the blood cholesterol figure to 320 mg. (normal, 160). In rabbits it was raised to 260 mg. (normal, 40) by feeding cholesterol. In one instance, by feeding 1 gm. of cholesterol per day for several days, the figure reached 395 mg.

A general survey of the effects of cholesterol feedings makes it clear that a hypercholesterolemia may be readily induced—particularly in rabbits, but also in other animals. Fats may not be substituted. The effect on the blood cholesterol figure appears promptly, i. e., within twenty-four hours, and likewise disappears rather promptly (in two or three days).

All of the foregoing results were secured by feeding cholesterol. We have found one report in which the feeding of alcohol is considered to have effected an increase. Bürger and Schweisheimer [16] fed two young dogs with 33 c.c. of alcohol in a 10 per cent. solution, and noted a rise in one instance of 12.5 per cent. This took place within twenty-four hours, beyond which time the examinations were not continued. Their conclusions are not convincing to us, for in one instance they withdrew 230 c.c. of blood from one animal within thirty-two hours, which introduced a large element of uncertainty. Furthermore, a variation of 12.5 per cent. is within the limits of technical error, or at least means little as cholesterol determinations go, even when the Windaus technic was employed.

SUBCUTANEOUS INJECTIONS

Little has been done by this route. Lehmann [17] injected a cholesterol-oil mixture in 10 c.c. doses under the skin of rabbits. The maximum amount of cholesterol appeared in the blood between the third and sixth days, i. e., much less promptly than in the feeding tests already cited.

14a. Jaffe, R. H., and Levinson, S. A.: Am. Rev. Tuberc. **11**:218, 1925.

15. Leupold, E., and Bogendorfer, L.: Deutsch. Arch. f. klin. Med. **140**:28, 1922.

16. Bürger, M., and Schweisheimer, W.: Ztschr. f. d. ges. exper. Med. **5**:136, 1916.

17. Lehmann, E. P.: J. Biol. Chem. **16**:495, 1913.

Whereas he analyzed the blood, he did not record the figures, apparently because he was uncertain as to their value.

Wacker and Hueck's [4] tables show that with 92 mg. as the normal figure for rabbits, an increase of but 6 mg. resulted after five subcutaneous injections of cholesterol, totaling 3.5 gm.

Corper [18] believes, and his work would indicate, that cholesterol is absorbed poorly from the skin (contra Aguilar [19]). He analyzed the skin of guinea-pigs at the injection sites in arriving at his conclusion, and he performed no blood analyses. Whereas his figures would make it follow that he did not induce a hypercholesterolemia, there is still the possibility that he did, for there is the suspicion that the introduction of cholesterol can stimulate the body tissues to an increased (endogenous) production. Thus, analyzing the entire carcasses of cholesterol-fed mice, Dezani [20] reports a grand increase of cholesterol—far above the amounts which were fed.

On the whole, so little has been done by the subcutaneous route that we are not warranted in pronouncing on its usefulness as an avenue for producing a hypercholesterolemia. The case is not proved. Theoretically, there are no contraindications, although in practice Basten [21] reported that cholesterol produced sloughing when injected into the ear and the back of dogs. Sloughing did not take place in the ten animals which we worked on, and in several of these goodly quantities of dry cholesterol crystals were purposely spilled into the margins of the laparotomy wound and were enclosed there in the final suturings.

INTRAVENOUS INJECTIONS

In introducing cholesterol into the blood, the foremost obstacle is the vehicle. Watery agents are not promising, and such solvents as ether are incompatible with the circulating blood. Ordinary emulsion in physiologic sodium chlorid becomes packed in the injection needles as a result of the physical peculiarities of cholesterol. If the emulsion is made in an oil, the oil introduces possibilities of embolism or of fat metabolic upset which may complicate the experiment. Nevertheless, a number of workers (Adler,[22] Klotz,[23] etc.) have injected oil emulsion, particularly in attempts to induce atheroma; here the association of neutral fats was not of moment. Cholesterol analyses were not reported in conjunction with these, and while it is obvious that a hypercholesterolemia was induced, we have no idea of the degree or the duration.

18. Corper, H. J.: J. Exper. Med. **21**:181, 1915.
19.—Aguilar, R.: Boll. d. Soc. di. Nat. in Napoli. Ser. 2. **2**:94, 1908-1909.
20. Dezani, S.: Arch. di farmacol. sper. **12**:4, 1914.
21. Basten, G.: Virchow's Arch. f. path. Anat. **220**:176, 1915.
22. Adler, A.: J. Exper. Med. **26**:581, 1917.
23. Klotz, O.: J. Med. Res. **33**:157, 1915.

Kaethe Dewey [24] has met the technical difficulties by making a colloidal preparation which met her indications and was free from these oil objections. She made intravenous injections into some of her rabbits with a 1 per cent. emulsion in doses of 5 to 10 c.c. at varying intervals. Two rabbits received as many as twenty-seven injections over a period of 108 days. The specimens of blood were examined once only, i. e., just prior to the death of the animals, and if we take 129 mg. as her normal for whole blood,[25] there was an increase of from 50 to 250 per cent. She gives no idea of how long the hypercholesterolemia persisted, but she believes that it was temporary.

We have prepared some of Dewey's emulsion, and it is admirable so far as injection purposes are concerned. Under the microscope some of the cholesterol appeared in the form of minute acicular crystals, i. e., it was not a colloidal preparation pure and simple. We did not inject it into our animals, because our problem required a more permanent hypercholesterolemia than the emulsion promised.

We conclude that when other fatty factors in the economy do not contraindicate, cholesterol may be injected intravenously in an oily emulsion. If the experiment requires that cholesterol only be injected, Dewey's emulsion fulfils the requirements; but in any case, the hypercholesterolemia is temporary.

INTRAPERITONEAL INJECTIONS

This avenue is especially appealing because the quantities introduced can be relatively large (particularly in dealing with small animals like rats and mice), because absorption is so certain, the dosage is exact, and because at necropsy the site of application which is to be inspected for tissue effects is such a definite and accessible structure, i. e., a surface.

Ellis and Gardner [26] injected an olive oil-cholesterol emulsion (1.0 gm. of cholesterol) into one rabbit, and olive oil only as a control into the peritoneal cavity of another rabbit. A few days later the two blood cholesterols showed 84.9 and 61.1 mg. of cholesterol, respectively, a definite increase. They did not report figures for normal animals, but the rabbit which received the olive oil only may be accepted as such.

Using her colloidal preparations already mentioned, Dewey obtained results from intraperitoneal injections similar to those following injections of blood.

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24. Dewey, K.: Arch. Int. Med. **17**:757, 1916.

25. Dewey, K.: Arch. Int. Med. **17**:764, 1916.

26. Ellis, G. W., and Gardner, J. A.: Proc. Roy. Soc. London **85**:385, 1912.

AUTHORS' EXPERIMENTS

Our own work has been confined to this intraperitoneal avenue, but since we desired a more enduring hypercholesterolemia, we had to forego Dewey's emulsion. We felt that the largest particles possible should be used, assuming that a certain amount of reactive fibrosis would occur around them and that this barrier would retard and prolong absorption; that is, we aimed to create a cholesterol depot in the peritoneal cavity.

We used Merck's chemically pure product as representing the most staple article available. The crystals were sterilized in the autoclave, and about 0.5 gm. was poured or tapped directly into the peritoneal cavities of two monkeys, two dogs, two cats, two rabbits and two guinea-pigs through small laparotomy openings. Blood cholesterol determinations were made at weekly (nearly) intervals thereafter for three weeks, and subsequently at intervals of about two weeks. Details

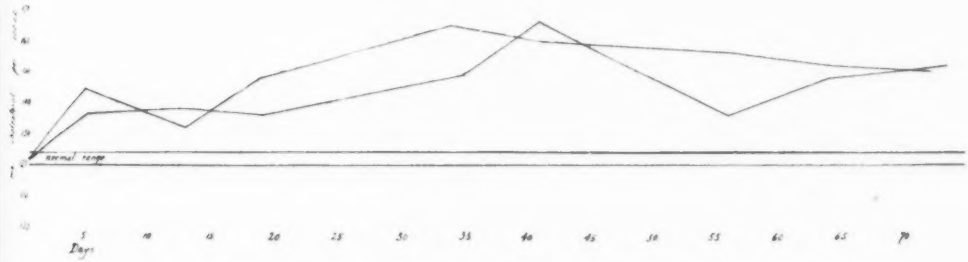

Chart 1.—Experiments on monkeys. Highest figure was on fortieth day, differing from other species tested; peak of increase about 35 per cent.; mean, 25 per cent. There was less disposition for the figure to return to normal than in the other animals.

of the chemical technic and dietary considerations are recorded in the preceding communication.

The charts bring out that, considering the several animal species as a whole, a definite hypercholesterolemia was induced within five days,[27] roughly averaging 25 per cent. At first (end of five days) the figure was very high, but was wholly irregular in the different species, i. e., from 33 to 200 per cent. above normal. Thereafter there was a sudden drop and then a steady decline, the normal not being approached until six to ten weeks. Thus, in the matter of permanence of hypercholesterolemia, we may consider it to have been induced to the extent

27. Doubtless this took place promptly, i. e., within a few hours. It was impossible to follow the blood effects in detail on account of the danger of exsanguinating the animals, or at least inviting a hydremia which would distort the cholesterol values.

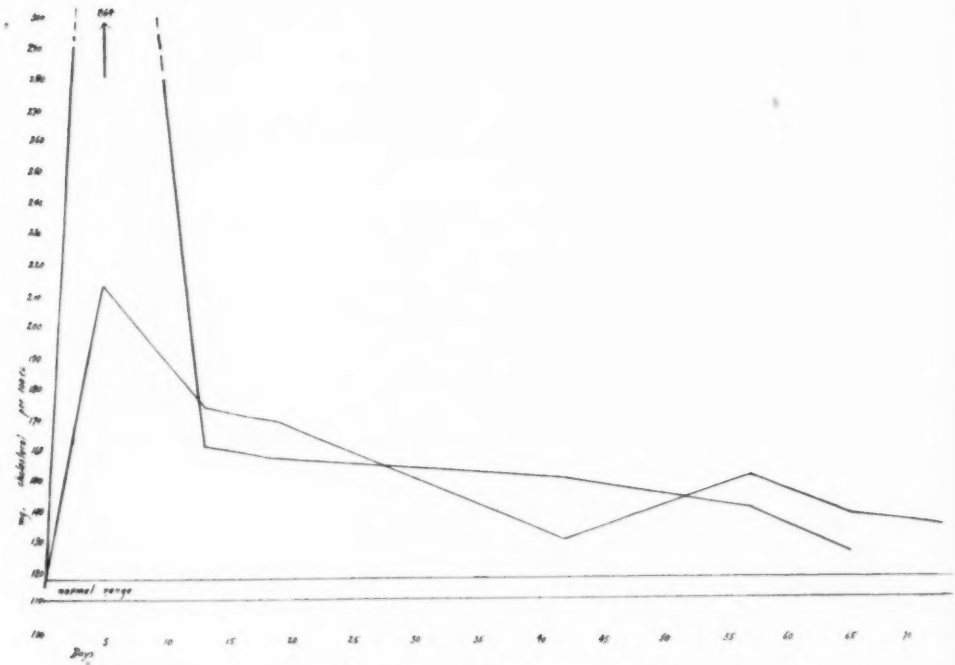

Chart 2.—Experiments on dogs. The tremendous 200 per cent. increase at first was not equaled by the other species. Mean level may be put at 25 per cent. increase.

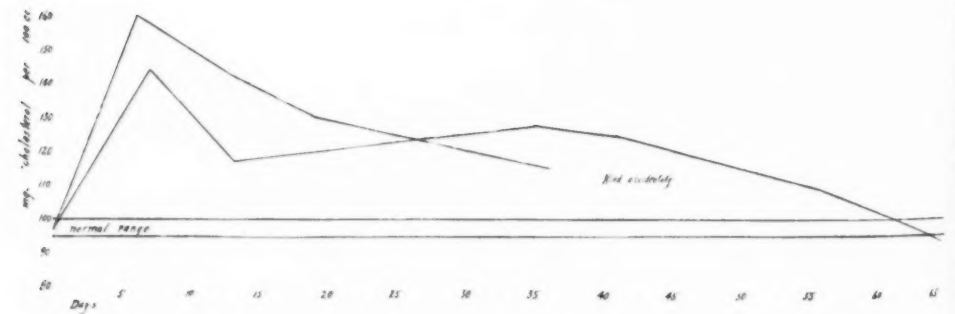

Chart 3.—Experiments on cats. At the five day peak the increase was 60 per cent. The average thereafter may be put at 25 per cent.

of 25 per cent. for six weeks when the crystals were introduced intraperitoneally.

Comparing the several species of animals, it appears that in point of steadiness of the hypercholesterolemia induced, the monkey ranks first. In intensity, the rabbit excels, its mean being about twice as high as that of any of the other species. This is referable more to the low normal figure than to the absolute cholesterol content. For extremely high figures of but brief duration the dog stands apart from the others.

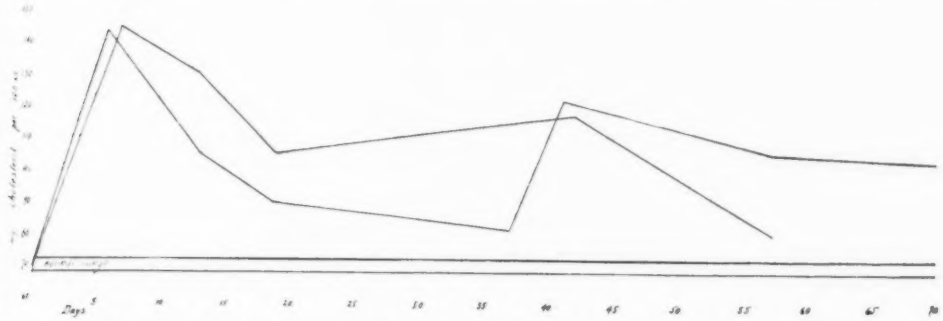

Chart 4.—Experiments on rabbits. At the five day peak the increase was 100 per cent., and the mean increase thereafter 50 per cent.

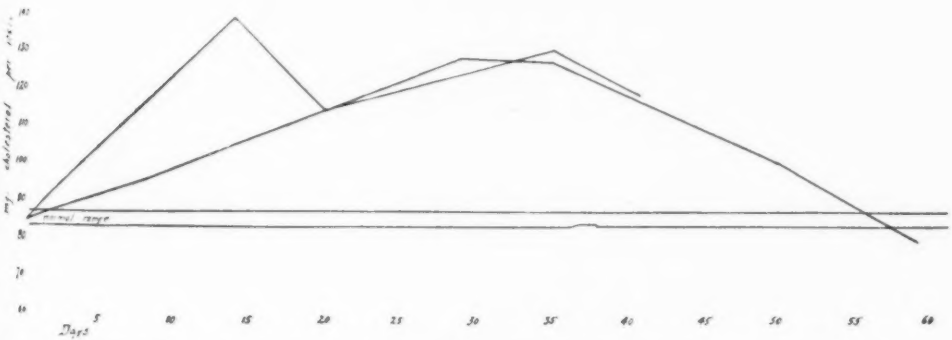

Chart 5.—Experiments on guinea-pigs. At the peak the increase was 60 per cent. The mean was 30 per cent.

Since at the death of these animals there were no traces of cholesterol or of important tissue reaction in the peritoneal cavity, we surmise that much greater ranges and permanence of hypercholesterolemia might be secured under other experimental conditions. Thus, in retrospect, we believe that we would have secured these had we used three or four times as much cholesterol and molded it into solid lumps after melting. We would thus have secured, we feel, the more extreme grades of hypercholesterolemia which we desired, and an even slower absorption of the cholesterol and more prolonged hypercholesterolemia.

CONCLUSIONS

Reports of chemically controlled hypercholesterolemias in the various experimental animals are surprisingly rare in the literature, giving scant basis for general conclusions. Of the common laboratory animals, the rabbit appears to be the most susceptible to experimental hypercholesterolemia and has been the most extensively used. As Luden intimates, this may be the expression of the herbivorous animal. If so, the rabbit should not be considered as the ideal experimental animal when comparing results with human disease, even though it be the animal of choice for inducing a hypercholesterolemia.

On oral feeding, a hypercholesterolemia may be induced in rabbits with almost any substance rich in cholesterol. Neutral fats do not suffice.

Subcutaneous injections have not had a fair trial as controlled by blood analyses.

The intravenous route may be employed, using either oil to emulsify the cholesterol, or the emulsion of Dewey. The hypercholesterolemia thus induced is temporary (determined in rabbits only).

The intraperitoneal route provides a hypercholesterolemia of 25 per cent. lasting up to six weeks, provided coarse crystals are used.

LACQUER DERMATITIS TREATED WITH RHUS TOXICODENDRON ANTIGEN

REPORT OF A CASE

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The genus *Rhus* contains four species which are recognized as capable of producing toxic symptoms when applied to the skin of susceptible persons. These are *Rhus venenata,* swamp or poison sumac; *Rhus toxicodendron* (*Rhus radicans*), the ordinary poison ivy; *Rhus diversaloba,* the poison oak of the Pacific slope, closely allied to *Rhus toxicodendron;* and *Rhus vernicifera,* the lacquer plant of Japan and China. The first of these, *Rhus venenata,* is confined to the eastern part of North America; the second, *Rhus toxicodendron,* is found over large parts of North America. So far as I know, it does not occur in western North America, its place there being taken by *Rhus diversaloba. Rhus vernicifera* occurs native only in eastern Asia, and with it is said to grow another poisonous species, but whether this is *Rhus toxicodendron* or *Rhus diversaloba* I do not know.

The eruptions produced in susceptible persons by all the American species are identical. *Rhus venenata* is said to be the most violent, but I have no conclusive evidence on this point. Poisoning by *Rhus vernicefera* has been recognized in the Orient for centuries, being a common occurrence in men engaged in preparing lacquer, especially in those new to the trade. The descriptions given are lacking in detail, but they give one the impression of an eruption showing more redness and less swelling or vesiculation than are seen in severe poison ivy cases. In this country, cases have been reported following the handling of mah jong boxes and tiles, and these are described as being identical in appearance with cases of ivy poisoning. The treatment in the whole group of cases, until the last few years, was purely expectant, consisting of the application of soothing lotions until the patient recovered, presumably by developing a temporary immunity; the time required varied from a few days to two or three weeks. With the introduction of *Rhus toxicodendron* antigen, a method became available by means of which even severe attacks could be brought to a termination within a few days. The antigen is now prepared both from *Rhus toxicodendron* and from *Rhus venenata,* and it is claimed that each drug is effective only against poisoning from the same species as that from

which the drug was prepared. However, it is also claimed that *Rhus venenata* antigen is used extensively and successfully in the West, where *Rhus venenata* does not occur, so it is evident that further investigation is required.

It is particularly in connection with this question of the identity of the poison occurring in different species of *Rhus* that the following case is of interest.

REPORT OF A CASE

Miss K. W., aged 32, a trained nurse, on April 22, 1925, when she consulted me, presented on her right arm below the insertion of the deltoid and the upper half of the right forearm, a typical picture of rhus poisoning, with great swelling and intense itching followed by burning. The entire surface was covered with close-set vesicles, some large, some small. There was no fever, but the discomfort and general distress were great, and the patient was incapacitated. She said that she had been subject to severe attacks of ivy poisoning since childhood, the attacks often lasting three or four weeks. On Sunday, April 12, for the first time she had put on a bracelet of lacquer. She had worn it on the upper arm, and she had moved it repeatedly up and down over the elbow. Itching was first noticed the next day, and soon a vesicular dermatitis appeared, which gradually increased, until the time of her visit. She had continued her work in the operating room during the first few days of the eruption, scrubbing up every day. It is a matter of conjecture whether this was beneficial by removing some of the poison or harmful because of the irritation produced. She stopped work, and used soothing lotions and salves, without any real benefit. A lotion containing boric acid and camphor water gave as much relief as anything. Judging by her past experience, she expected a week or two more of suffering, and then a gradual convalescence. She was given an injection of 0.7 c.c. *Rhus toxicodendron* antigen, undiluted, in the right buttock. Next day the swelling was much reduced, the skin at the bend of the elbow was drying, and the burning sensation had disappeared. The general skin surface was irritable, with slight dermographia, but there were no new vesicles. She then received 1 c.c. of antigen diluted with 0.5 c.c. of sterile water in the right deltoid muscle. Following this, recovery was rapid. On the third day, April 24, she began taking 5 minims (0.3 c.c.) tincture of *Rhus toxicodendron* by mouth, three times a day. The injections were somewhat painful, especially that in the buttock, but the patient was most emphatic in her statement that the pain of the injection was as nothing in comparison with the distress produced by the eruption.

COMMENT

The case is unique; there is no other report of the treatment of lacquer dermatitis with *Rhus toxicodendron* antigen. As far as it goes, it is evidence in support of the belief that the poisonous principle in *Rhus vernicifera* is the same as that in *Rhus toxicodendron,* and strong evidence that *Rhus toxicondendron* antigen may be useful in any form of rhus poisoning.

FUNGUS INFECTIONS OF THE SKIN

REPORT ON CULTURAL STUDY OF FLORA OF RINGWORM *

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MONTREAL, CANADA

This report is based on the investigation of a series of 140 cases of ringworm seen at the dermatologic clinic of Dr. G. Gordon Campbell, at the Montreal General Hospital, during a period of approximately a year and a half.

Early in the investigation, in some cases we were not able to obtain the causative fungus in culture, but with growing experience, our results in this respect have very much improved.

The methods used have been those outlined by Sabouraud.[1] Initial cultures from hairs, scales, etc., have usually been readily obtained on glycerin agar. When necessary, numerous plants have been made to ensure the isolation of the fungus in pure culture. The plan of drying the scales or hair stumps for a few days in sterile test tubes, particularly when taken from moist areas, has been found extremely helpful in retarding or preventing the growth of associated bacteria.[2] Cultures for complete identification of the fungus have been grown on Sabouraud's 4 per cent. glucose agar and 3 per cent. peptone agar (using French peptone [Chassaing] and pure glucose).[3] Giant cultures have been made in Erlenmeyer flasks and also in dessert dishes.[4]

We have made the microscopic study of the growths both by means of direct smears and by growing the fungus in a hanging drop preparation using a 4 per cent. glucose bouillon as medium.

A number of cases were investigated in which a remote possibility of fungus origin was considered. In none of these cases in which careful

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* From the Dermatological and Pathological Departments of the Montreal General Hospital.

* This work was made possible by the aid of a grant from the Cooper Memorial Fund, McGill University.

1. Sabouraud, R.: Les Teignes, Paris, Masson et Cie, 1910.

2. Mitchell, James Herbert: Further Studies of Ringworm of the Hands and Feet, Arch. Dermat. & Syph. **5**:174 (Feb.) 1922.

3. Weidman, Fred D., and Millan, Thomas M.: A Comparison of Ingredients of Ringworm Culture Mediums with Special Reference to American and French Crude Maltose, Arch. Dermat. & Syph. **4**:451 (Oct.) 1921.

4. Burgess, J. F.: A Method of Growing and Preserving Giant Cultures of Ringworm Fungi for Teaching Purposes, J. Intern. A. of Medical Museums and J. of Technical Methods, Bull. No. 11, May 4, 1925, p. 61.

The table gives the details of the positive cultures.

Positive Cultures

Genera of Positive Cultures:

	Cases
Microsporon	46
Trichophyton	34
Epidermophyton	3
Achorion	8
Saccharomyces	8
Total	99

Tinea capitis:

	Cases
Microsporon audouinii	18
Microsporon lanosum	15
Microsporon felineum	5
(3 cases showed lesions of the glabrous skin)	
Microsporon tardum	1
Microsporon fulvum	2
Trichophyton cerebriforme	1
Trichophyton crateriforme	1
Trichophyton violaceum	5
Trichophyton plicatile	1
Trichophyton polygonum	1
Tr. microides denticulatum	1
Tr. microides farinulentum	1
Tr. microides granulosum	1
Tr. gypseum	1
Achorion schönleinii	8
Total	62

Tinea barbae:

	Cases
Trichophyton rosaceum	1
Trichophyton microides-granulosum	1
Trichophyton faviforme-album	1
Total	3

Epidermophytosis (Lesions affecting the glabrous skin):

	Cases
Microsporon lanosum	3
Microsporon audouinii	2
Trichophyton acuminatum	1
Trichophyton violaceum	3
Trichophyton plicatile	2
Trichophyton rosaceum	1
Trichophyton microides-asteroides	2
Trichophyton microides-granulosum	1
Trichophyton microides-farinulentum	2
Trichophyton faviforme-discoides	1
Epidermophyton inguinale	3
Trichophyton gypseum	5
Saccharomyces	8
Total	34

microscopic examination of the hair or scales was negative for mycelium or spores were we able by cultural methods to demonstrate a causative fungus. But two cases of trichophytic granuloma yielded pure cultures of *Trichophyton* from the pus, although we could not demonstrate the fungus in the pus contents. The fact, pointed out by Sabouraud and many other observers, that the same fungus may produce clinically different types of lesions in different persons, and further, that practically identical clinical lesions may be caused by different fungi, has been amply borne out by our observations here.

In all, 140 cases have been investigated. Of these, 130 cases showed the presence of a ringworm fungus by microscopic examination, and ten cases were negative. In sixteen cases, in which the microscopic examination was positive, we were unable to isolate the fungus. We have, therefore, obtained 114 positive cultures, of which fifteen have, as yet, been unidentified. Of the ninety-nine identified cultures, sixty-two were obtained from cases of ringworm of the scalp, thirty-four from lesions of the glabrous skin, and three from cases of ringworm of the beard.

The clinical condition to which Fabry [5] gave the name "erosio interdigitalis blastomycetica," and on which Greenbaum and Klauder [6] and Mitchell [7] contributed valuable articles, has been of not infrequent occurrence in our clinic. Of 130 undoubted cases of ringworm infection, this condition has been observed in ten cases. Clinically the appearance was that of an eroded lesion with a peripheral margin of macerated, undermined epithelium, occurring in the webs of one or more interdigital spaces of the hand. All of our patients were women. Microscopically, the epithelium in seven of our cases showed simply strands of broken mycelium, whereas in three cases, a sparse amount of mycelium and numerous grapelike clusters of spores were present. We were able to obtain pure cultures of saccharomyces in eight of these cases.

We were not able to demonstrate the presence of a fungus of the ringworm variety on normal skin. Cultures were made from scrapings of normal or slightly macerated epithelium from the skin between the fourth and fifth toes in 100 patients seeking relief for some other skin lesion. In no case did we obtain a positive culture of a variety of a ringworm fungus. Apparently a ringworm fungus is rarely present on the skin surfaces without causing definite and characteristic reactions.

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5. Fabry: München. med. Wchnschr. **49**:1557, 1917.

6. Greenbaum, S. S., and Klauder, Joseph: Yeast Infections of the Skin, Arch. Dermat. & Syph. **5**:332 (March) 1922.

7. Mitchell, James Herbert: Erosio Interdigitalis Blastomycetica, Arch. Dermat. & Syph. **6**:675 (Dec.) 1922.

The following cases are cited in which lesions of a typical dyshidrosis developed, apparently resulting through the dissemination of spores of the causative fungus from an obvious primary focus.

CASE 1.—A girl, aged 17 years, with an eruption on each hand, presented herself at the Clinic. She said the eruption had started about three weeks previously. On the palmar surface of the right hand, over the metacarpophalangeal joints of the second and third fingers, there was an inflammatory, eroded area, approximately 1 inch (2.5 cm.) in diameter. The edges were sharply defined and easily detached, and long strands of mycelium, in some cases breaking up to form chains of spores, were easily demonstrated. On the sides of the fingers of both hands, over the remainder of the palm of the right hand and on the dorsum of the left hand were numerous typical sago-grain-like vesicles with little or no inflammatory areola. Repeated searchings of the vesicular roofs failed to disclose any trace of the fungus. Culturally the fungus was shown to be *Trichophyton asteroides.*

CASE 2.—A man, aged 42, presented eroded macerated lesions between the toes and a few discrete vesicles on the dorsum of the toes of both feet. Microscopic examination showed abundant mycelium in the scales and in the roofs of many of the vesicles. Treatment was instituted with Whitfield's ointment (salicylic acid, 4 per cent., and benzoic acid, 5 per cent.). Nine days later, he developed numerous vesicles on both soles and on the palms and the sides of the fingers. Strands of degenerated mycelium could be seen microscopically in the roofs of the vesicles on the soles, but repeated searching failed to disclose a fungus in the lesions of the hands. Seven days later he developed an eruption on the thighs and upper arms, most marked on the extensor aspects, and slightly so on the back. The eruption consisted of coin and pea-sized areas made up of small red papules, capped by a tiny scale, and situated for the most part at the follicular orifices. There was slight itching. These lesions were those of *Lichen trichophyticus.* Culturally, the fungus was the pleomorphic variety of *Epidermophyton inguinale.* Agglutination tests of the patient's serum against the spores of the organism were negative in dilutions of 1 : 50, 1 : 100, 1 : 200 and 1 : 300.

Comment.—In each of these cases there developed lesions of a dyshidrotic character, associated with, and apparently due to, an obvious focus of ringworm infection. It would seem probable that many cases of dyshidrosis, excluding those due to obvious chemical or physical causes, are of mycotic origin. In the absence of a demonstrable primary focus of entry of the organism, it is difficult, and frequently impossible, to demonstrate the presence of a ringworm fungus as an etiologic agent.

SUMMARY

1. The incidence of the varieties of ringworm infections occurring in the dermatologic clinic of the Montreal General Hospital, based on the identification of ninety-nine positive cultures, is reported.

2. Of sixty-two cases of scalp ringworm, 60 per cent. were due to *Microsporon* infections, 50 per cent. of which were about equally divided between *Microsporon audouinii* and *Microsporon lanosum;*

25 per cent. were due to *Trichophyton* infections, and about 15 per cent. to *Achorion schönleinii*.

3. Of thirty-four cases of epidermophytosis, 12 per cent. were of *Microsporon* origin, 60 per cent. due to *Trichophyton* varieties, and 22 per cent. to *Saccharomyces*.

4. Three cases of tinae barbae were all due to members of the *Trichophyton* family.

5. Two cases of epidermophytosis are reported, in each of which lesions of dyshidrosis developed following a primary mycotic infection. In one of these cases, lesions of *Lichen trichophyticus* were also present.

VALUE OF NONSPECIFIC PROTEIN THERAPY IN SYPHILIS

WITH SPECIAL REFERENCE TO ITS EFFECT ON THE WASSERMANN REACTION WHEN USED AS AN ADJUNCT TO NEO-ARSPHENAMIN *

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AND

CARROLL S. WRIGHT, M.D.

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In a previous communication,[1] the authors showed that nonspecific therapy favorably influences the courses of syphilis. It was demonstrated that injections of a 4 per cent. suspension of milk protein in the deep muscles would result in partial or complete involution of some types of secondary and tertiary manifestations of the disease. It was not intimated that injections of a foreign protein are in any way a cure for syphilis, but it was suggested that perhaps the effect of the injections is to stimulate the natural protective forces of the body, which, if true, would indicate that such a therapeutic procedure, in conjunction with other therapy, might prove of value.

The procedure, as carried out, consisted of a preliminary course of six intramuscular (gluteal) injections of a 4 per cent. sterile suspension of milk protein, the injections being given at intervals of two or three days. Upon the completion of the course of milk protein injections, the patients received a series of injections of neo-arsphenamin at weekly intervals, blood being withdrawn each time for a Wassermann test.

In order to determine whether the use of nonspecific therapy as an adjunct to other and more powerful antisyphilitic remedies is of any real value, the studies of the writers along this line were continued. In addition to employing the nonspecific protein therapy in secondary and tertiary cases, a number of patients with latent syphilis were treated by the method outlined above. In all, twenty-five patients with latent syphilis were treated in this manner. These patients presented no evidence of syphilis other than a positive Wassermann reaction. For comparison, twenty-five patients with latent syphilis who were being treated by neo-arspenamin alone, were studied at the same time. No attempt was made to select the cases for one group or the other, but they were used just as they entered the clinic. It was our purpose to

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* Contribution from the Department of Dermatology-Syphilology, Graduate School of Medicine, University of Pennsylvania.

1. Greenbaum, S. S., and Wright, C. S.: Effects of Nonspecific Protein Therapy in Syphilis, with Special Reference to Its Cutaneous Manifestations, Arch. Dermat. & Syph. **10**:551 (Nov.) 1924.

see whether, as we had shown that this form of therapy alone would influence the cutaneous manifestations of syphilis, it would hasten the reversal of a positive Wassermann reaction to a negative reaction when combined with a more powerful antisyphilitic drug.

Tables 1 and 2 show definitely that nonspecific therapy alone will favorably influence the course of cutaneous syphilis. In secondary

TABLE 1.—*Effect of Milk Protein on Secondary Cases*

	Clinical Type of Eruption	Effects of Six Injections of 4 Per Cent. Suspension of Milk Protein
1	Generalized maculopapular eruption; palmar lesions; annulopapular lesions on face	75 per cent. of eruption involuted after six injections of milk protein
2	Generalized polymorphous eruption with papular lesions predominating; general malaise	Malaise disappeared after two injections of milk protein; eruption improved
3	Maculopapular eruption; papulosquamous lesions on face and annulopapular lesions on palms	Lesions of face 75 per cent. involuted; palmar lesions disappearing
4	Arciform syphilids on cheeks.....	Lesions considerably improved after three injections of milk protein; markedly improved by six injections; completely healed on left cheek
5	Annulopapular eruption.....	Lesions on face improved after three injections of milk protein; marked improvement after six injections
6	Secondary follicular syphilis generalized; debilitated	Patient's general condition much improved after two injections of milk protein; cutaneous lesions but slightly improved by six injections
7	Annular papular eruption, marked on face	Lesions show beginning involution after three injections of milk protein; almost involuted after six injections

TABLE 2.—*Effect of Milk Protein in Tertiary Cases*

	Clinical Type of Lesions	Effect of Milk Protein
1	Nodular and ulcerative gummas of right leg	Focal reaction after first injection; lesions much improved after six injections; ulcers healing
2	Crusted ulcers and nodular gummas of right elbow	Some lesions healed after three injections of milk protein; all lesions healed after six injections
3	Syphilitic keratosis of palms; annular nodular lesion on wrist	Complete involution of lesions after six injections
4	Syphilitic keratosis of right hand.....	Complete involution of lesions after six injections
5	Tertiary syphiloderm of left palm.....	Ninety per cent. involuted after sixth injection
6	Ulcerating gummas of right breast of three years' duration; marked secondary infection	Lesions partially healed after six injections of milk protein, but infection continued
7	Nodulo-ulcerative gumma of tip of nose.	Lesion 75 per cent. healed after six injections
8	Syphilitic hyperkeratosis of the right palm	Complete involution of lesions after six injections

syphilis it was generally noted that the lesions showed some involution after two or three injections of the protein, and in a number of cases 75 per cent. of the lesions had involuted after the sixth injection. Tertiary lesions responded even more favorably. In only one instance did a gummatous lesion refuse to heal, and in this instance the lesion was complicated by a severe secondary pus infection. These facts are offered merely to show the influence of the procedure on the course of

syphilis. Nonspecific therapy is not required in hastening the involution of the cutaneous manifestations. We feel that the condition in which it might be of the greatest service is latent syphilis with a strongly positive Wassermann reaction as an only symptom. It is well known that in such cases considerable difficulty may be encountered in obtaining a negative Wassermann reaction. In Table 3 are outlined the results obtained in treating patients with this type of case with combined non-

TABLE 3.—*Latent Syphilis Treated with Milk Protein and Neo-Arsphenamin*

No.	Wassermann Test Before Treatment	No. of Injections of Neo-Arsphenamin Necessary to Obtain Negative Wassermann Test	Final Result	Wassermann Test Unchanged
1	Strongly positive.....	..		15*
2	Strongly positive.....	9	Negative complement-fixation reaction	
3	Strongly positive.....	14	Negative complement-fixation reaction	
4	Strongly positive.....	1	Reversed to positive after 3 months	
5	Strongly positive.....	2	Patient left clinic after single negative Wassermann reaction	
6	Strongly positive.....	..	Patient disappeared after sixth injection of neo-arsphenamin	6*
7	Moderately positive..	4	Negative after three months	
8	Strongly positive.....	1	Negative complement-fixation reaction	
9	Strongly positive.....	6	Wassermann reaction reversed itself several times during course of injections	
10	Strongly positive.....	5	Negative complement-fixation reaction	
11	Moderately positive..	3	Patient lost sight of after tenth neo-arsphenamin injection; Wassermann reaction still negative	
12	Strongly positive.....	3	Negative complement-fixation reaction	
13	Strongly positive.....	3	Negative complement-fixation reaction	
14	Strongly positive.....	..	Patient lost sight of after 4 neo-arsphenamin injections	4*
15	Strongly positive.....	3	Patient lost sight of after 9 neo-arsphenamin injections; still negative	
16	Strongly positive.....	..		10*
17	Strongly positive.....	6	Wassermann reaction again reversed to a positive	
18	Strongly positive.....	7	Negative complement-fixation reaction	
19	Strongly positive.....	2	Wassermann reaction again reversed to a positive	
20	Strongly positive.....	..		15*
21	Moderately positive..	3	Wassermann reaction still negative after 12 injections	
22	Strongly positive.....	8	Patient lost sight of after 11th injection of neo-arsphenamin; still negative	
23	Strongly positive.....	..		13*
24	Strongly positive.....	..	Patient disappeared after 6 injections	6*
25	Strongly positive.....	..	Patient disappeared after 8 injections	8*

* Neo-arsphenamin injections.

specific and specific therapy, while in Table 4 are tabulated the results obtained from injections of neo-arsphenamin alone. It is from a study of Table 5 that we can best draw conclusions as to the value of nonspecific protein therapy in hastening the disappearance of a positive Wassermann reaction.

Twenty-five patients were treated in each series, no attention being paid to the duration of the disease or to the amount of treatment previously given, but only to the strength of the Wassermann test as estimated by the Kolmer method, and only those cases showing a strongly positive or moderately positive Wassermann reaction being used. The

majority of the cases on first examination showed a strongly positive Wassermann reaction. It will be seen on referring to Table 5 that in seventeen of the patients treated with neo-arspenamin and milk protein the reaction became negative, while it became negative in only twelve of those treated with neo-arspenamin only —the percentage becoming negative being, respectively, 68 per cent. and 48 per cent. In other words, 20 per cent. more cases became negative after combined therapy than after neo-arsphenamin. Only four of those treated with neo-arsphenamin and milk protein com-

TABLE 4.—*Latent Syphilis Treated with Neo-Arsphenamin Alone*

No.	No. of Neo-Arsphenamin Injections Required to Obtain a Negative Wassermann Reaction	Final Outcome	Failed to Obtain a Negative Reaction at Any Time	Number of Injections Given
1	4	Again reversed to positive	..	18
2	..	.....	+	17
3	23	Wassermann reaction again became moderately positive; reversed to a negative after 30th injection of neo-arsphenamin	..	30
4	2	Wassermann reaction soon reverted to a positive again	..	25
5	..	.....	+	28
6	..	.....	+	15
7	1	Reverted to a positive	..	15
8	3	Permanently (?) negative after 8 neo-arsphenamin injections	..	..
9	12	Reverted to a positive	..	15
10	12	Patient disappeared after a single negative	..	15
11	..	.....	+	28
12	6	Reverted to a positive	..	15
13	..	.....	+	18
14	2	Reverted to a positive		
15	..	.....	+	21
16	..	.....	+	12
17	..	.....	+	20
18	..	.....	+	13
19	4	Reverted to a positive after 8 injections; then became permanently (?) negative	..	..
20	10	Reverted to a positive	..	15
21	..	.....	+	12
22	..	.....	+	13
23	..	.....	+	21
24	10	Never again became positive	..	26
25	..	.....	+	35

bined and giving a negative reaction once were positive on final analysis. Of the twelve cases which became negative after neo-arsphenamin only, seven were positive again on final analysis. In other words, the negative phase was considerably less stable when treatment consisted of neo-arsphenamin alone. Thus, if we readjust the totals of cases negative in final analysis in both columns, there would be thirteen in which the treatment was combined therapy as compared with five in which treatment was neo-arsphenamin. It is, of course, manifestly impossible to speak of a persistently negative complement-fixation test, as the studies are less than a year old, but a much shorter time is required to obtain a negative phase with the combined than with the straight therapy.

In some cases long-continued treatment with combined milk protein and neo-arsphenamin, and with neo-arsphenamin alone failed to affect the Wassermann reaction. It is possible that more intense study of these cases might reveal obscure lesions of the viscera or central nervous system. It is seen that the failures were less with combined therapy than with neo-arsphenamin therapy alone.

There is a striking difference in the average number of injections of neo-arsphenamin required to produce a negative phase of the Wassermann reaction. When combined nonspecific and specific therapy were employed, the average of the number of injections given before a negative was obtained was 4.7, while where specific therapy alone was used, 7.5 injections were required on the average.

This series of cases is not large, but the results obtained seem to indicate that nonspecific therapy is of distinct value as an adjunct to

TABLE 5.—*Summary of Results*

	Milk Protein and Neo-Arsphenamin	Neo-Arsphenamin Alone
Number of cases	25	25
Negative Wassermann reaction obtained in	17	12
Percentage of cases in which negative Wassermann reaction obtained	68%	48%
Cases in which negative Wassermann reaction reverted to a positive	4	7
Cases remaining persistently negative	13	5
Failed to obtain negative Wassermann reaction	9	13
Average number of injections of neo-arsphenamin needed to obtain a negative Wassermann reaction	4.7	7.5
Average number of injections of neo-arsphenamin given in cases in which there was a failure to obtain a negative Wassermann reaction	8.5	20.0

neo-arsphenamin therapy. To know just how much value it possesses would require a comparison with the results obtained with combined neo-arsphenamin and mercury, and neo-arsphenamin and bismuth. Studies along these lines are in progress. There is a tendency at present to seek methods of stimulating the natural protective mechanisms of the body in the treatment of syphilis. There is some reason to believe that injections of protein have this action.

It is well known that a rise of temperature alone suffices to hasten the involution of cutaneous manifestations of syphilis. It is not uncommon for intercurrent acute infectious diseases to have a distinct effect on the manifestations of syphilis. This effect may be apparent in delaying the onset of secondary eruptions or in hastening the involution of skin lesions already present. The benefits of fever are not limited to cutaneous manifestations. The improvement noted in cases of paralysis following the inoculation of the patient with malarial organisms is thought to depend largely on the fever produced, and Piltz and Mattauschek, in reviewing a large series of cases of late syphilis in which the

disease was of many years' standing, found that more than 100 asymptomatic cases gave a history of fever-producing sickness shortly after the original infection, while none of those showing symptoms of paralysis gave similar histories.

The general reaction produced by intramuscular injections of 5 c.c. of a 4 per cent. suspension of milk protein is slight, and is rarely perceptible to the patient. Although no records were kept of the temperature changes in this series of cases, we know from the studies of others that a milk injection does call forth a certain degree of febrile reaction. Schmidt and Kaznelson [2] found that a rise of temperature occurred usually in from six to eight hours and persisted for from eight to twelve hours. The explanation of this fever varies with the author.

There is also an increase of leukocytes following the injection of milk. Schmidt and Kaznelson grouped the leukocytic reaction that follows milk injection into three classes. They observed first a group in which a primary leukopenia was followed by a leukocytosis consisting largely of polymorphonuclear neutrophils; a second group in which a leukocytosis was already present, and the injection resulted in a decrease in the number of neutrophils; a third group in which the reaction consisted chiefly in an increase in the number of mononuclear elements. Muller [3] found that myelocytes were thrown into the circulation in abundance, indicating a marked stimulation of bone marrow. Other workers have found an increase of oxidation, of catalysis and a mobilization of enzymes and antibodies.

Using these facts as a basis, together with clinical experience, Wenhardt [4] has evolved the theory that when we make use of nonspecific therapy we stimulate all the cells of the organisms to greater activity in the production of either specific substances, antibacterial in character, or merely increase the general resistance to intoxication by speeding up the mechanism of detoxication. This stimulation does not involve any alteration in function. The organism by nonspecific reaction acquires no new method of defense, and probably does not overcome infection or intoxication through agencies other than those always at its disposal; but the stimulation represents a summation, a cumulative effort of the defensive agencies of all the organs.

This theory, as evolved by Wenhardt, would satisfactorily explain the favorable action protein therapy has in syphilis. There is a tendency on the part of writers of the present day (Stokes, Lesser) to attribute the therapeutic action of mercury in syphilis to an effect in stimulating

2. Schmidt and Kaznelson: Ztschr. f. klin. Med. **33**:18, 79 and 275, 1916.
3. Muller: Med. Klin. **14**:440, 1918.
4. Wenhardt, A., quoted by Peterson: Protein Therapy and Nonspecific Resistance, New York, The Macmillan Co., 1922.

the natural protective mechanism of the body against the disease rather than to any direct effect on the spirochete. Bismuth is said to have a similar action. Levaditi and Nicolau [5] have shown that bismuth in contact with a tissue extract exerts a greater therapeutic power than when the drug alone is used. Theoretically, this is combined protein drug therapy.

SUMMARY

In this study we have shown that nonspecific protein therapy alone will result in partial or complete involution of secondary and tertiary lesions. When used as an adjunct to neo-arsphenamin in the treatment of patients with latent syphilis with strongly positive Wassermann reactions, the influence in reducing a positive reaction to negative is more marked than when neo-arsphenamin alone is used. The explanation of this is not clear, but it is suggested that the protein therapy serves to stimulate normal protective mechanisms within the body. If this is true, nonspecific protein therapy should prove a valuable adjunct to the usual antisyphilitic remedies.

1714 Pine Street—1402 Spruce Street.

5. Levaditi and Nicolau: Ann. de l'Inst. Pasteur **38**:3, 1924.

Abstracts from Current Literature

Syphilitic Elephantiasis of the Scrotum. C. H. Marshall, J. A. M. A. **85**:875 (Sept. 19) 1925.

Marshall reports a case of this rare manifestation of syphilis. His patient was a negro, aged 30, who gave a history of a penile lesion thirteen years before the onset of the scrotal condition. The result of a Wassermann reaction was four plus, The penis and scrotum were greatly enlarged, and the latter was studded with rounded and warty protuberances. The microscopic picture was typical of elephantiasis. Cultures and sections stained for bacteria were negative. There was improvement following antisyphilitic therapy.

The Treatment of Thrush with Gentian Violet. H. K. Faber and L. B. Dickey, J. A. M. A. **85**:900 (Sept. 19) 1925.

These authors used a 1 per cent. aqueous solution of gentian violet painted on the mucous membrane not oftener than once a day. In fourteen cases, seven were cured with one application, and the remainder in from two to five days.

Livedo Reticularis. C. M. Williams and H. Goodman, J. A. M. A. **85**:955 (Sept. 26) 1925.

The authors record cases of persistent mottling of the skin in two children of the same family. Unable to satisfy themselves as to the category in which these cases belong and struck by the indefiniteness of the classification of the livedo group, they have reviewed this subject and attempted a clarification of it. They propose three groups: (1) cutis marmorata, designating a transitory mottling occurring on exposure to cold and probably the result of imperfect vasomotor control; (2) livedo reticularis iodiopathica in which mottling is permanent. Reported cases show a marked variation in the quantity and arrangement of the discoloration. The one constant pathologic change is vascular dilatation. (3) Livedo reticularis symptomatica, in which inflammatory changes are demonstrable. The commonest class in this group is erythema ab igne. Both tuberculosis and syphilis may cause this condition.

In all cases there must necessarily be some cutaneous anomaly of the blood-vessels. This anomaly may govern the distribution of eruptions due to other causes, notably tuberculosis and syphilis.

Radium (Mesothorium) Necrosis. F. L. Hoffman, J. A. M. A. **85**:961 (Sept. 26) 1925.

A series of cases of necrosis of the jaw apparently as the result of occupational radium exposure are recorded, included among which are four deaths. The patients were all operatives in a luminous watch dial plant. The luminous paint used contained a minute quantity of radium or mesothorium. The operatives pointed their brushes by moistening it with their lips, and in this way conveyed a small quantity of the material to the mouth. Necrosis of the jaw bone, accompanied by anemia, developed months or several years later. Hoffman's investigation lead to the conclusion that this occupation is dangerous only when the habit of pointing the brush with the lips obtains.

Michael, Houston, Texas.

LUPUS PERNIO. W. DUBREUILH and P. JOULIA, Ann. de dermat. et syph. **5**:689 (Dec.) 1924.

Three cases are reported, with histologic studies. In two, only the face was involved. Roentgenographic studies of the chest, and of the extremities in the case in which they were affected, are offered as evidence that the trouble is systemic.

CUTANEOUS HISTOPATHOLOGY. PAUTRIER and G. LEVY, Ann. de dermat. et syph. **5**:700 (Dec.) 1924.

The authors outline their observations, especially in the case of xanthoma, and conclude that there exists in the skin a trophic system, a peripheral expansion of the reticulo-endothelial system of Ribbert-Goldmann-Aschoff, made up of a cellular network uniting the vascular endothelium to the epidermis by way of the perithelial and dermic cells and the anastomosing cells of Langerhans. In view of its trophic function, as well as its apparent function of pigment formation, the authors have called it the trophomelanic network.

SUBCUTANEOUS CALCAREOUS CONCRETIONS AND THYROID-OVARIAN INSUFFICIENCY. MATHIEU-PIERRE WEIL and R. WEISSMANN-NETTER, Ann. de dermat. et syph. **5**:724 (Dec.) 1924.

A case is reported in which the concretions were especially rich in phosphates. The calcium content of the blood was found to be normal, but there was an increase in phosphoric acid. The illustrations consist of roentgenograms.

TREATMENT OF TROPICAL PHAGEDENIC ULCERS. VIGGO GENNER, Ann. de dermat. et syph. **5**:733 (Dec.) 1924.

The author discourages the use of arsenical preparations, and reports good results from the local use of iodoform, U. S. P. Yaws does not respond to iodoform, and can thus be differentiated.

ERYTHEMA INDURATUM (BAZIN). J. NICOLAS, J. GATÉ and P. RAVAULT, Ann. de dermat. et syph. **6**:1 (Jan.) 1925.

After careful histologic study, the authors report two cases in which the important lesions were vascular. The arterial vessels were involved rather than the venous.

EPIDERMOMYCOSES, WITH THE PRESENTATION OF SIX NEW PARASITES. LEE MCCARTHY, Ann. de dermat. et syph. **6**:19 (Jan.) 1925.

Working in Sabouraud's laboratory, McCarthy had studied the characteristics of these new organisms, which he describes in detail, with illustrations. They are *Epidermophyton clypeiforme*, of the monomorphic group, and *Epidermophytons plurizoniforme, lanoroscum, gypseum* and *niveum* of the multiform group and finally *Trichophyton rotundum*. *Epidermophyton lanoroscum* was found in a case of generalized infection, while the other five produced lesions of the pseudodyshidrotic type.

CONFLUENT AND GENERALIZED HYPERKERATOSIS DUE TO ARSPHENAMIN. JOSE MAY, Ann. de dermat. et syph. **6**:55 (Jan.) 1925.

A case is reported which indicates that neo-arsphenamin can cause melanodermic and keratotic lesions when administered repeatedly over a long period, and that arsenical keratosis can be generalized instead of being limited to the hands and feet.

ABNORMAL LICHENIFICATIONS: HYPERTROPHIC OR GIANT LICHENIFICATION. PAUTRIER, Ann. de dermat. et syph. **6**:81 (Feb.) 1925.

The parts usually involved in these cases are the scrotum, labia majora, inguinal folds, proximal third of the thighs, hips and axillary folds. The lesions are considerably elevated, vegetating and sometimes of cerebriform appearance, simulating mycosis fungoides and epithelioma, and giving rise to grave errors in diagnosis. Itching is always present. Four cases are described, clinically and histologically, with good photographs and photomicrographs.

GENERAL INFECTION WITH THE GONOCOCCUS: GONOCOCCIC MENINGITIS AND GONOCOCCIC PURPURA. BRUUSGAARD and THJOTTA, Ann. de dermat. et syph. **6**:114 (Feb.) 1925.

In sections of the affected skin the organisms were found in blood vessels, and a few could be found in the cells of the dermal infiltration. The organisms were also found in the spinal fluid.

HYPERKERATOTIC LICHEN CORNEUS WITH ERYTHRODERMA, LICHEN PLANUS AND BUCCAL LICHEN PLANUS. HENRI MALHERBE, Ann. de dermat. et syph. **6**:129 (Feb.) 1925.

A case is reported in which the lesions of prurigo nodularis and lichen planus coexisted, in support of the theory that both have the same origin. A biopsy could not be obtained.

GENERALIZED ZOSTER AND ITS GANGRENOUS VARIETIES. C. LAURENTIER, Ann. de dermat. et syph. **6**:134 (Feb.) 1925.

Truly generalized (not multiple) zoster exists, but is very rare, according to Laurentier, who reports a case in a man working with cyanamid, an arsenical compound.

RADIODERMIC ULCER. DUBREUILH and DAVID-CHAUSSE, Ann. de dermat. et syph. **6**:161 (March) 1925.

In 1922, an ulcer developed in a patch of atrophic skin where a recurrent basal cell epithelioma had been treated by roentgen rays on several occasions from 1913 to 1920. Skin grafting was performed, and following this traumatism the ulceration recurred. In another case, in which uterine fibromas had been irradiated nine years previously, an ulcer appeared in the patch of atrophic and telangiectatic skin. Histologic studies of both cases are reported.

ELIMINATION OF BISMUTH IN THE URINE IN THE TREATMENT OF SYPHILIS WITH SOME ORDINARY PREPARATIONS OF BISMUTH. SVEND LOMHOLT, Ann. de dermat. et syph. **6**:170 (March) 1925.

From his studies the author concludes that the oily suspensions are absorbed much more slowly than the corresponding aqueous suspensions, from two to seven times more slowly during the first fourteen days. Among the oily suspensions, during the first fourteen days the elimination of the tartrobismuthate is almost double that of iodo-quinio bismuth, which, in turn, is eliminated nearly twice as rapidly as the hydroxid. During the first fourteen days, about three fourths of the bismuth, injected in aqueous solution, is eliminated. With the tartrobismuthate, the maximum is reached on the second day, with the iodo-quinio bismuth, on the third or fourth day, and with the hydroxid, on the fifth to the seventh day.

Bowen's Disease of the Mucosae: The First Three Cases. L. Richon, Ann. de dermat. et syph. **6**:191 (March) 1925.

The clinical and histologic aspects of the cases are described, with histologic sketches. In each case, the mucosa of the vulva and vagina was involved, and the age of the patients ranged from 55 to 65 years.

Keratoma or Keratoderma, Punctiform or Miliary and Diffuse Palmar and Plantar Keratoderma with Miliary Keratomas. F. Balzer, Ann. de dermat. et syph. **6**:225 (April) 1925.

Balzer describes Matsumoto's case and Sweitzer's, both called keratoderma punctatum, and adds two of his own; in one the lesions were situated in apparently normal skin, while in the other there was a diffuse palmar and plantar keratoderma as a background. The latter is considered the more usual type. According to Balzer, the occurrence of small vesicles may precede the appearance of the craters in some cases. He feels that the condition is due to infection.

Zosteriform Achromia. C. Audry, Ann. de dermat. et syph. **6**:244 (April) 1925.

Since birth or early childhood, the patient, a woman, aged 33, had presented a widespread melanoderma and patches of complete depigmentation unilaterally in the ninth dorsal segment. Audry feels that in these patches the melanoblasts are absent, and that, inversely, they are augmented in the melanodermic areas.

Protein Therapy in Dermatology. J. Golay and A. Starobinsky, Ann. de dermat. et syph. **6**:248 (April) 1925.

Having used this treatment in cases of pustular acne, furunculosis, pyoderma, sycosis, cold abscess, suppurating trichophyton infection, zoster, psoriasis, erythroderma, eczema and several pruritic affections, the authors conclude that it is useful in dermatology, although the results are variable, and sometimes the cures are transient.

Prurigo of Besnier. H. Haxthausen, Ann. de dermat. et syph. **6**:312 (May) 1925.

In a study of thirty-eight cases, twenty-four of which occurred in males, the author has found that this diffuse prurigo is a chronic disease, with sharp exacerbations, often seasonal, usually beginning in early infancy. The face, extremities and neck were found to be the sites of predilection, and lesions were never found on the scalp. The lichenified patches in the cubital and popliteal regions are regarded as characteristic. Often there is also bronchial asthma or hay-fever, and ichthyosis is a common complication. Cutaneous sensitization tests often have suggested the proper therapy.

Brocq's Disease (Erythrodermie Pityriasique en Plaques Disseminées). A. Kissmeyer, Ann. de dermat. et syph. **6**:378 (June) 1925.

Eight cases are summarized, of various duration, in patients from 7 to 35 years of age. Calcium chlorid was administered, and the eruption completely disappeared in three cases and was benefited in two others. The author considers it a well defined eruption, having no apparent relationship with the other conditions classified in the parapsoriasis group. In view of its histologic characteristics and response to calcium therapy, he feels that it somewhat resembles lichen planus, psoriasis and erythema multiforme.

PIGMENTATION OF THE SKIN FOLLOWING TREATMENT WITH ARSENIC AND BISMUTH. VLADIMIR FELDMANN, Ann. de dermat. et syph. **6**:386 (June) 1925.

During a second series of injections of neo-arsphenamin, a transient pruritic erythema developed, and after bismuth had been given, as well as neo-arsphenamin and glucose, pigmented patches appeared within three months on the trunk and thighs. Although no bismuth could be found in excised specimens, the author is of the opinion that the coloration was due to a deposit of a bismuth salt, probably the sulphid, in the skin, at the sites of the previous arsenical erythema.

THE PLURALITY OF THE SYPHILITIC ORGANISMS: A GENERAL CRITICAL REVIEW. CLEMENT SIMON, Ann. de dermat. et syph. **6**:289 and 392 (May and June) 1925.

In the author's opinion, the theories of Levaditi and Marie, of L. Fournier and Schwartz are extremely seductive, but they have not been conclusively demonstrated, and the clinical arguments appear insufficient. It is suggestive that rabbit spirochetosis seems to resemble the disease produced by the neurotropic organism, but for a conclusive demonstration it appears that experiments with man and monkeys are necessary, and not with rabbits.

ICONOGRAPHIC STUDY OF THE STAPHYLOCOCCIC PUSTULE AND LESIONS DERIVED FROM IT. R. SABOURAUD, Ann. de dermat. et syph. **6**:353 and 417 (June and July) 1925.

In a well-illustrated article, which cannot well be abstracted, Sabouraud describes the bacterial and defensive activities in these lesions. To account for the occurrence of furuncles and abscesses side by side, he supposes that when a large number of organisms is present, an abscess is likely to form, whereas, other things being equal, a smaller number would give rise to furuncle formation, with suppuration rather than slough formation.

A DYSKERATOTIC DERMATOSIS OF MENINGEAL AND RADICULAR ORIGIN. CONSTANTIN ILIESCO and TRAJAN POPESCO, Ann. de dermat. et syph. **6**:450 (July) 1925.

Following a fever, symmetrical apparently parakeratotic plaques appeared on a man's trunk and upper and lower extremities. Meningismus was present. Histologic study revealed the presence of dyskeratosis in the patches.

LATE CHRONIC MENINGITIS DUE TO CONGENITAL SYPHILIS. G. ETIENNE, L. MATHIEU and M. VERAIN, Bull. Soc. franç. de dermat. et syph. **32**:R.N.3, 1925.

In a woman, aged 37, with skeletal stigmas of congenital syphilis, there had been continuous severe headache. The diagnosis was established by examination of the spinal fluid.

A CASE OF CANITIES. CORRET and CARILLON, Bull. Soc. franç. de dermat. et syph. **32**:R.N.6, 1925.

In a man, aged 31, the hair of the scalp, beard and eyebrows had become white within three weeks. Alopecia areata was present, and might have accounted for the canities.

LINEAR LICHEN PLANUS OF THE FOREARM. J. WATRIN, Bull. Soc. franç. de dermat. et syph. **32**:R.N.8, 1925.

A typical eruption, of five months' duration, resisting arsenical medication, was treated by exposure of the interscapular region to intensive unfiltered roentgen rays (5 Holzknecht units), after which the pruritus diminished considerably.

SYPHILITIC GUMMA OF THE STERNUM AND GENERALIZED MELANODERMA. SPILLMANN and DROUET, Bull. Soc. franç. de dermat. et syph. **32**:R.N.11, 1925.

In a man with vagabonds' disease, there were pigmented patches in the mouth, possibly of endocrinous origin, as well as gumma of the sternum.

IS SYPHILIS DECREASING? L. SPILLMANN, Bull. Soc. franç. de dermat. et syph. **32**:R.N.14, 1925.

Under the effective treatment used during the war, syphilitic infection became less frequent, but, according to the author, the number of fresh cases is now increasing. He would attribute this increase to lax and ineffective courses of treatment now commonly employed.

PAGET'S DISEASE. P. MASSON, Bull. Soc. franç. de dermat. et syph. **32**:R.S.6, 1925.

With the aid of illustrative photomicrographs, Masson seeks to support his claim that Paget's disease should be considered as an epidermotropic cancer, and not as one of the dyskeratoses. According to Masson, the epithelioma invades the epidermis from the underlying tissues.

DYSKERATOSIS. PAUTRIER and G. LEVY, Bull. Soc. franç. de dermat. et syph. **32**:R.S.19, 1925.

The authors support the contentions of Masson, with the feeling that dyskeratosis is an unimportant manifestation.

PAGET'S DISEASE OF MAMMARY ORIGIN. HICKEL, Bull. Soc. franç. de dermat. et syph. **32**:R.S.29, 1925.

A woman, aged 55, had had an erosion about the left nipple for six months. It presented the clinical and histologic characteristics of Paget's disease, and a glandular epithelioma was found invading the epidermis. The findings in this case are offered to support the contentions of Masson and Pautrier, mentioned above.

A CASE OF LUPUS-CARCINOMA. J. ROEDERER and METZGER, Bull. Soc. franç. de dermat. et syph. **32**:R.S.33, 1925.

When the patient was 17 years old, lupus vulgaris appeared on the right cheek. After several years, it was cauterized, and later neglected entirely. At the age of 34, the patient noticed tumor formation; the tumor was excised, and did not reappear until twenty-four years later. It was then found to be a prickle cell epithelioma.

A LARGE ULCERATING AND DESTRUCTIVE BASAL CELL EPITHELIOMA OF THE FACE. PAUTRIER and LEVY, Bull. Soc. franç. de dermat. et syph. **32**:R.S.35, 1925.

An extensive epithelioma of twelve years' duration, involving the orbit, had resisted previous irradiation, but responded favorably to intensive radium applications.

A Case of Erythematous Anetoderma. Gaston Weill, Bull. Soc. franç. de dermat. et syph. **32**:R.S.38, 1925.

A plaque of five years' duration was present on the arm of a woman, aged 30. The etiology was obscure, the patient apparently being healthy. The case was considered as answering Jadossohn's description of erythematous anetoderma.

The Lymph in the Pathology of Cutaneous Diseases. Samberger, Bull. Soc. franç. de dermat. et syph. **32**:R.S.40, 1925.

Considering disturbances of lymphatic secretion, Samberger describes the conditions attending the various forms of urticaria and pemphigus and mentions the variety of etiologic factors. Anomalies of lymph circulation are also discussed, including epidermolysis bullosa, elephantiasis, eczema and erythema multiforme, it being emphasized that in the last two conditions a variable amount of inflammation is always present, accounting for changes in the picture.

Ulcer of the Leg. Pautrier, L. Ambard, F. Schmid and G. Levy, Bull. Soc. franç. de dermat. et syph. **32**:R.S.52, 1925.

In a patient with hyperglycemia but no glycosuria and in one with normal blood sugar findings, an ulcer of the leg was healed by insulin medication. In both cases the ulcers were of long standing in middle-aged women. The first case is presented to illustrate the value of blood sugar estimation. In connection with the second case, the question arises as to whether insulin may not have some hitherto unknown action in stimulating healing by modifying the nutrition of the tissues.

Remarks on the Preceding Communication. L. Ambard and F. Schmid, Bull. Soc. franç. de dermat. et syph. **32**:R.S.55, 1925.

In view of the possible power of insulin to increase tissue nutrition and hasten healing, the authors suggest its use in nondiabetic patients whose lesions are resistant to treatment.

Urticaria Pigmentosa of Late Onset. Pautrier, Bull. Soc. franç. de dermat. et syph. **32**:R.S.57, 1925.

In a woman, aged 36, the eruption had first appeared at the age of 22, two months after childbirth. The blood picture was normal, and the possibility of leukemia was excluded.

Lupus-Carcinoma. J. Roederer and G. Levy, Bull. Soc. franç. de dermat. et syph. **32**:R.S.62, 1925.

A woman, aged 57, presented extensive lupus vulgaris of the face, of about fifty years' duration. Arising from the lesion on the left cheek, there was a crusted tumor with the histologic picture of prickle cell epithelioma.

Tuberculids of the Face. Pautrier, Bull. Soc. franç. de dermat. et syph. **32**:R.S.63, 1925.

A man, aged 38, in apparently good general health, had first noticed the lesions on the forehead four months previously, the rest of the face and the hairborder being subsequently involved in successive outbreaks. The serologic reactions were negative for syphilis, and there was no response when bismuth

was administered. The diagnosis of tuberculid was confirmed histologically. The tuberculids were a form intermediate between acinitis and miliary lupoid. A rabbit was inoculated and died.

SLUGGISH ULCERATION CURED BY INSULIN, IN A PATIENT WITH NORMAL GLYCEMIA. PAUTRIER, AMBARD, SCHMID and LEVY, Bull. Soc. franç. de dermat. et syph. **32**:R.S.73, 1925.

A vegetating tuberculous ulceration of the foot healed readily when insulin was administered. Numerous other measures had been tried previously, without benefit.

TWO RARE CASES OF CUTANEOUS LESIONS PROVOKED BY CHEMICAL SUBSTANCES. G. SACKENREITER, Bull. Soc. franç. de dermat. et syph. **32**:R.S.75, 1925.

In both cases there was severe dermatitis and necrosis, essence of vinegar having been applied in one and powdered arsenic to the other.

SUBACUTE PEMPHIGUS WITH EXTENSIVE BULLAE IN A CHILD. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **32**:R.S.77, 1925.

The patient, a child, aged 5, was first seen by the author with a bullous eruption of four days' duration on the face and in the mouth. A few bullae subsequently appeared elsewhere, and there was fever and malaise. Silver compounds were applied to the denuded areas, and recovery ensued. Only staphylococci were found in the lesions. Keratitis was produced by inoculation in one rabbit, and reproduced by transfer to the cornea of another rabbit.

ERYTHEMA INDURATUM (BAZIN). PAUTRIER and G. LEVY, Bull. Soc. franç. de dermat. et syph. **32**:R.S.85, 1925.

Painless nodules had been appearing on the legs of a girl for a year; they showed the gross and histologic picture of erythema induratum. Although no Koch bacilli could be found, inoculation of a guinea-pig was followed by the appearance of induration and lymph node enlargement.

PAPULOPUSTULAR ACNE WITH KELOID FORMATION AND ATROPHIC COMEDONES. PAUTRIER, METZGER and G. LEVY, Bull. Soc. franç. de dermat. et syph. **32**:R.S.87, 1925.

The eruption, which in places simulated macular atrophy, was of seven years' duration, in a man, aged 24. The original process was perifollicular inflammation.

GIANT LICHENIFICATION AND CIRCUMSCRIBED NODULAR LICHENIFICATION IN THE SAME PATIENT. PAYENNEVILLE and CASTAGNOL, Bull. Soc. franç. de dermat. et syph. **32**:R.S.89, 1925.

The condition, involving the left knee, leg and thigh of a negro had been present for ten years, with constant severe itching. The features described by Pautrier in the *Annales* (1922) were present.

SYMMETRICAL ADENOMA SEBACEUM OF THE FACE AND RECKLINGHAUSEN'S DISEASE. PAYENNEVILLE, Bull. Soc. franç. de dermat. et syph. **32**:R.S.92, 1925.

In a girl, aged 10 years, adenoma sebaceum of the type described by Pringle co-existed with von Recklinghausen's disease, both conditions having first appeared at about the same. The same was true of a young soldier, who presented lesions of the Hallopeau type.

NEW RESEARCH CONCERNING THE STREPTOBACILLUS OF DUCREY. J. HABABOU-SALA, Bull. Soc. franç. de dermat. et syph. **32**:R.S.96, 1925.

The author isolates cultures of the organism from washed lesions, these cultures having the typical gross and microscopic characteristics and producing positive intradermal reactions in patients. A suspension of the organisms is filtered and sterilized, and when this is applied daily to the lesions there is rapid involution, without untoward reactions, in the absence of any other treatment.

SYPHILITIC CHANCRE RESISTING ARSENIC AND BISMUTH AND RAPIDLY CURED BY MERCURIC CYANID. LEVY and METZGER, Bull. Soc. franç. de dermat. et syph. **32**:R.S.111, 1925.

Although the dark-field examination was negative, the histologic picture was that of a syphilitic chancre; when the patient had first come under observation, a roseola had been present. The possibility of a complicating chancroidal infection or poradenolymphatis was also excluded; there was extraordinary lymph node involvement.

CUTANEOUS TUBERCULOSIS, NODULAR AND ULCERATIVE, IN THE REGION OF THE KNEE. PAUTRIER and METZGER, Bull. Soc. franç. de dermat. et syph. **32**: R.S.115, 1925.

Present for 11 years in a man, aged 32, these lesions were of unusual appearance, although histologically tuberculous. The patient had pulmonary tuberculosis and also tuberculous laryngitis and epididymitis.

HYPODERMAL SARCOIDS OF THE FACE, OF ATROPHIC TENDENCY. PAUTRIER and ROBERT, Bull. Soc. franç. de dermat. et syph. **32**:R.S.119, 1925.

In a woman, aged 47, the condition was of five years' duration, the entire face being involved, with patches of hypodermal infiltration. A histologic report is included.

GUMMATOUS AND FISTULOUS TUBERCULOSIS OF THE REGION OF THE VAGINA AND THE INGUINAL FOLD. LEVY, GLASSER and SLOIMOWICI, Bull. Soc. franç. de dermat. et syph. **32**:R.S.124, 1925.

There was no internal involvement, but the external genitals were extensively affected. The diagnosis of tuberculosis was established by guinea-pig inoculation.

ULCER OF A LEG IN A WOMAN WITH NORMAL BLOOD SUGAR FINDINGS CURED BY LOCAL DRESSINGS OF INSULIN POWDER. PAUTRIER, SCHMID and ROBERT, Bull. Soc. franç. de dermat. et syph. **32**:R.S.132, 1925.

A palm-sized ulcer on the leg of a woman, aged 90, healed in 15 days under applications of insulin mixed with a diluting powder.

LICHEN SCROFULOSORUM, REMARKABLY PRURITIC AND SIMULATING LICHEN PLANUS. PAUTRIER, Bull. Soc. franç. de dermat. et syph. **32**:R.S.133, 1925.

An eruption appearing in a child, aged 2½ years, with a chronic cough, presented elements highly suggestive of lichen planus, in groups, but the histologic diagnosis was lichen scrofulosorum.

Eczema and Eczematids. A. Civatte, Bull. Soc. franç. de dermat. et syph. **32**:R.S.134, 1925.

In a well illustrated article, the author describes the histology of these conditions, including the "seborrheids" and the psoriasiform parakeratoses, with particular emphasis on the feature of small vesicle formation.

Shock Due to Arsphenamin, with Abortion Following. P. Merklen, M. Wolf and A. Neel, Bull. Soc. franç. de dermat. et syph. **32**:R.S.148, 1925.

Four hours after the third of a series of injections of arsphenamin, there was a chill, with headache and nausea, and flushing of the skin. This reaction subsided, and seventeen days later another dose of the drug was given, followed by a violent reaction and abortion.

Results of Surgery of the Sympathetic Nervous System in Scleroderma. R. Leriche, M. Wolf and R. Fontaine, Bull. Soc. franç. de dermat. et syph. **32**:R.S.153, 1925.

Sclerodactylia of fourteen years' duration was benefited by section of the peri-arterial sympathetic nerve, and removal of the superior cervical ganglion or section of its roots seemed to improve facial scleroderma.

Alopecia Areata. Levy-Franckel and Guillaume, Bull. Soc. franç. de dermat. et syph. **32**:144, 1925.

Alopecia areata with spasm of the arterioles and polyuria, following traumatism and other evidences of sympathetic and endocrinous disturbances were demonstrated in a man, aged 49, who had suffered sudden loss of hair in 1908, following a wound in the leg. The alopecia having persisted.

Actinomycosis. Lortat-Jacob and Legrain, Bull. Soc. franç. de dermat. et syph. **32**:148, 1925.

The iodin content of colloidal iodin is said to be high, and it is well tolerated. A patient with a case of three months' standing was cured within three weeks by its administration.

Vaccinotherapy of Chancroid with Filtrates of Bacteria Associated with Bacillus of Ducrey. H. Jaussion and Diot, Bull. Soc. franç. de dermat. et syph. **32**:152, 1925.

Stock preparations of the most commonly associated organisms were used as moist applications and changed twice a day. Rapid cures were effected. The Ducrey bacillus was not employed.

Pruritic Angiosclerotic Purpura with Lichenoid Elements. Gougerot and Paul Blum, Bull. Soc. franç. de dermat. et syph. **32**:161, 1925.

In a man, aged 41, the condition has been present for fifteen months. On both legs, there were varicose veins, purpuric spots and small lichenoid papules, with intense pruritus.

Acute Dermatitis Herpetiformis with a Chronic Urinary Affection. Jeanselme and Hufnagel, Bull. Soc. franç. de dermat. et syph. **32**:163, 1925.

There was a generalized pruritic erythematous papular and bullous eruption, of one month's duration, in a man, aged 84 with an eosinophylia of 6 per cent.

CONJUGAL SYPHILIS OF ABORTIVE TYPE IN THE FEMALE. A. GALLIOT, Bull. Soc. franç. de dermat. et syph. **32**:165, 1925.

From previous observations the author concludes that this form of syphilis occurs typically in women. There are no cutaneous or mucous lesions, and the affection is benign, with slight chance of transmission except to the product of conception, toward which it has a toxic action.

OCCULT SYPHILIS OF WOMEN: GERM CARRIERS. LOUIS BORY, Bull. Soc. franç. de dermat. et syph. **32**:171, 1925.

The author feels that some women may become infected with syphilis through the inner surface of the menstruating uterus, or through the peritoneum, the organisms having gained access to it through the Fallopian tubes; in such cases the disease may remain latent and asymptomatic. He contends that women in apparently good health may be carriers of syphilitic infection, the disease being transmitted thus perhaps less frequently through intercourse than to products of conception.

SIGNIFICANCE OF CHROMATOPHILIC CORPUSCLES IN LESIONS OF PORADENIC MICROCHANCRE (DISEASE OF NICOLAS-FAVRE). LOUIS BORY, Bull. Soc. franç. de dermat. et syph. **32**:175, 1925.

In the subacute inguinal lymphogranulomatosis of Nicolas and Favre, the primary lesion is a plasmoma, in which these corpuscles are found. The author concludes that apparently they are degenerative forms of plasma cells, which may also be found in other conditions.

NONSUPPURATIVE VENEREAL INGUINAL ADENOPATHY (DISEASE OF NICOLAS AND DURAND). PAUL CHEVALLIER and PIERRE BARREAU, Bull. Soc. franç. de dermat. et syph. **32**:177, 1925.

The inguinal lymph node involvement appeared two weeks after intercourse, in a girl of 17 years. The spleen and other groups of lymph nodes were soon involved also. There was no eruption, the Wassermann reaction remained negative, and there were no evidence of Hodgkin's disease. The condition began to subside within two months, and had disappeared a month later. This was considered to be an atypical case of subacute inguinal lymphogranulomatosis.

TREATMENT OF CHANCROIDS BY THE VACCINE OF NICOLLE. W. DUBREUILH and P. BROUSTET, Bull. Soc. franç. de dermat. et syph. **32**:182, 1925.

In six of seven cases, satisfactory results were obtained, two or three injections usually being sufficient. The injections were given at intervals of from four to seven days. Rather severe temporary febrile reactions followed the injections.

HYPERTROPHIC LICHEN CORNEUS AND LICHEN PLANUS. J. MONTPELLIER, Bull. Soc. franç. de dermat. et syph. **32**:184, 1925.

Ten months after the first appearance of hypertrophic lichen corneus on the legs of a man, aged 30 lesions of lichen planus appeared in the buccal mucosa, indicating a possible relationship between the two conditions.

LICHEN PLANUS AND RADIOTHERAPY. J. MONTPELLIER and R. ZERAFFA, Bull. Soc. franç. de dermat. et syph. **32**:186, 1925.

Following the method of Pautrier and Hufschmitt, the authors irradiated both sides of the spine in the interscapular region and one side in the lumbosacral region. The lesions and the pruritus disappeared in the areas supplied by the irradiated regions, but persisted for two months in the untreated region.

POSTELEPHANTIASIC PERINEAL AND SCROTAL LYMPHANGIECTASES, WITH TRANSIENT EOSINOPHILIA. LÉRI and LAYANI, Bull. Soc. franç. de dermat. et syph. **32**:244, 1925.

The condition had been ushered in by acute febrile elephantiasis of the lower extremities, eleven years previously, and there had been subsequent exacerbations. A blood count showed the percentage of eosinophils to be eleven. Since the patient had never left France, the condition was apparently not of filarial origin.

TRANSMISSION OF MICROSPORON FELINEUM TO THE GLABROUS SKIN OF MAN. G. THIBIERGE, P. LEGRAIN and C. LEBLOIS, Bull. Soc. franç. de dermat. et syph. **32**:262, 1925.

Ten cases were observed, the eruption in some being rather extensive and resembling that of pityriasis rosea, while in others it was more limited. The organism was identified by Sabouraud. In the cat, the lesions are often faint and hard to find.

MILIARY PAPULAR LUPOID ACNE. MILIAN, Bull. Soc. franç. de dermat. et syph. **32**:267, 1925.

In cases of rosacea, to which this note refers, the author has often found apple jelly nodules under diascopic pressure, and he reports such a case in which improvement followed dietary care, with the use of a lotion, while histologic examination showed a tuberculoid structure.

A CASE OF SUBACUTE SCLERODERMA DURING CONVALESCENCE FROM CHOREA. LOUSTE, CAILLIAU and LECLERC, Bull. Soc. franç. de dermat. et syph. **32**:273, 1925.

In a girl, aged 15, there was an extensive and rapidly advancing scleroderma of three months' duration. She had just recovered from chorea, and menstruation had just been established.

THE ACTION OF INSULIN ON THE EVOLUTION OF PSORIASIS. RAVAUT, BITH and DUCOURTIOUX, Bull. Soc. franç. de dermat. et syph. **32**:275, 1925.

Three extensive cases were treated, and there was pruritus in all, which rapidly disappeared as the treatment progressed. The lesions had disappeared in from twenty-one to twenty-nine days. There was some recurrence of the lesions in two cases, one of which was treated again, effectively, with insulin. In one case there was hyperglycemia, while in the other two the blood sugar was about normal. The only local applications were alkaline baths.

A CASE OF LINGUAL CHANCROID. RAVAUT and DUCOURTIOUX, Bull. Soc. franç. de dermat. et syph. **32**:280, 1925.

In this case there were penile and lingual lesions, the latter being small and with no apparent lymph node involvement. Chancroids were produced on

the forearm by inoculation from these lesions, and while the lingual chancroid healed spontaneously in twelve days, the experimental lesion on the forearm was most rebellious to treatment.

Intolerance to Mercuric Cyanid Given Intravenously. Fouquet and Machtou, Bull. Soc. franç. de dermat. et syph. **32**:285, 1925.

Two cases are reported in which severe gastro-intestinal symptoms prevailed, and a third in which a bullous eruption appeared ten hours after the injection. In the third case, two courses of the cyanid had been given in 1906, with no reaction. The dosage used in each instance was small, and the injection was given slowly. Albuminuria was absent in the third case, and is not mentioned in the other two.

Cutaneous Manifestations in the Course of Treatment by Bismuth Alone or Associated with Mercury. Fouquet and Machtou, Bull. Soc. franç. de dermat. et syph. **32**:289, 1925.

In one case the eruption was urticarial, and in six erythematosquamous; it was often preceded by itching. The eruption usually appeared at the end of a series of injections, and it was impossible to state whether the mercurial or the bismuth compound was to blame. In several instances, there was a bismuth line on the gums, but never severe stomatitis, and in no case was there any sign of renal irritation.

A Case of Extensive Encystment Following Intramuscular Injections of Bismuth Hydroxid in Oily Suspension. H. Montlaur, Bull. Soc. franç. de dermat. et syph. **32**:294, 1925.

From January to March, 1925, a man had received eighteen injections; seventy-two days after the final treatment, swelling and inflammation were first noticed. An extensive incision was necessary.

The Gelovaccines: The Principle, the Technic and Advantages in the Treatment of the Pyodermas. Jausion and Diot, Bull. Soc. franç. de dermat. et syph. **32**:303, 1925.

Using peptonized gelose as a vehicle for application locally and organisms to correspond with the case, these workers secured good results in the treatment of sycosis, furunculosis, anthrax, lupoid sycosis, ulcerated lupus vulgaris and erosive gangrenous balanitis.

The Vaccine Therapy of Chancroid. Pautrier, Bull. Soc. franç. de dermat. et syph. **32**:189, 1925.

Referring to the work of Jausion and Diot, recently reported in this bulletin, Pautrier claims priority for the similar experiments of Hababou-Sala of Strasbourg.

Colloidal Iodin. Lafay, Bull. Soc. franç. de dermat. et syph. **32**:190, 1925.

According to Lafay, favorable opinions concerning the so-called colloidal iodin preparations are not justified, either in theory or in practice.

Two Cases of Sycosis Treated by Vaccine, Intradermally. Jean Meyer, Bull. Soc. franç. de dermat. et syph. **32**:195, 1925.

Good results were obtained by the use of high dosage, together with manual epilation.

Angiokeratomas of Mibelli. Hudelo, Caillaud and Chabrun, Bull. Soc. franç. de dermat. et syph. **32**:208, 1925.

In a girl, aged 13, who had had chilblains since early childhood, the keratotic lesions had been present on the dorsa of the hands and feet for about five weeks, the fingers and toes being involved. A histologic study is reported.

Lichen Spinulosus and Lichen Planus. Jeanselme and Burnier, Bull. Soc. franç. de dermat. et syph. **32**:211, 1925.

A woman, aged 61, complained of itching lesions of the back, of six months' duration. These lesions were typically lichen spinulosis. The buccal and vulvar mucosae showed patches of lichen planus. The histology of the lesions on the back was not that of lichen planus, and the author is inclined to accept the coexistence of the two eruptions as a coincidence.

Pityriasis Rubra Pilaris, Familial and Hereditary. Jeanselme and Burnier, Bull. Soc. franç. de dermat. et syph. **32**:215, 1925.

Mother and child presented a psoriasiform type of pityriasis rubra pilaris, which was also said to be present in another child of the family, and in two paternal cousins.

Generalized Favus. Louste and Le Clerc, Bull. Soc. franç. de dermat. et syph. **32**:218, 1925.

In a girl, aged 18, there was a favus infection of three years' duration, with nearly complete alopecia and widely scattered lesions over the body.

Lupus Pernio of the Lymphogranulomatous Type (Schaumann). Louste, Caillaud and Le Clerc, Bull. Soc. franç. de dermat. et syph. **32**:220, 1925.

In a girl, aged 22, poorly nourished, the nose and fingers were involved, and roentgenographic studies of the latter showed bone changes. The histologic structure resembled that of Boeck's sarcoid; the hypoderm was involved.

Ulcerative Tuberculosis of the Thigh. Louste, Caillaud and Marassi, Bull. Soc. franç. de dermat. et syph. **32**:225, 1925.

This disease occurred in a child, aged 10 years, the lesions somewhat resembling those of sporotrichosis. Histologic study brought the authors to the conclusion that the infection had come by way of the blood vessels.

A Case of Genital Erythroplasia of Chancriform Appearance, with Epithelioma. Louste, Caillaud and Marassi, Bull. Soc. franç. de dermat. et syph. **32**:227, 1925.

A stubborn penile ulcer of nearly a year's duration, in a patient aged 78, was examined histologically and found to correspond with a precancerous dermatosis (épithéliome papillaire nu) described by Darier in 1893, to which Queyrat, in 1911, had given the name of erythroplasia.

An Affection of Pemphigoid Course. Boucher, Bull. Soc. franç. de dermat. et syph. **32**:229, 1925.

During a period of two months, Boucher saw four of these cases in the same locality. In each case the eruption was at first purpuric, then pemphigoid and finally suppurative, with fever and a lethal outcome. The cause was not found.

ARSENICAL REACTIVATION OF SYPHILIS: ITS VALUE IN DIAGNOSIS, PROGNOSIS AND TREATMENT, ESPECIALLY IN EARLY CHANCRES. GASTOU and PONTOIZEAU, Bull. Soc. franç. de dermat. et syph. **32**:236, 1925.

In cases of suspected chancre, two injections of neo-arsphenamin were given at an interval of seven days, in a dosage of 0.15 to 0.3 gram; the Vernes test was then applied after ten and twenty days, and even after two or three months. The results in a series of 119 cases indicated that this procedure is valuable when the organisms cannot be found in the dark field, and particularly in the case of mixed infections.

PARKHURST, Toledo, Ohio.

HERPES ZOSTER AND SYPHILIS. M. ARTONE, Gior. ital. dermat. e syph. **66**:1044 (June) 1925.

The author reports six cases of herpes zoster probably due to syphilis. Herpes zoster may be produced by different infectious agents which attack the spinal or cephalic ganglions. In this series of cases there were also manifestations of neurosyphilis. The author remarks that a syphilitic patient suffering from herpes zoster must be suspected of having neurosyphilis.

A CASE OF SCLERODACTYLIA. A. DEVOTO, Gior. ital. dermat. e syph. **66**:1071 (June) 1925.

This is a report of a case of scleroderma and sclerodactylia in which marked endocrinous disturbances were found. The patient improved under mixed gland therapy.

INTRAVENOUS INJECTIONS OF BROMIDS IN THE TREATMENT OF DISEASES OF THE SKIN. C. FELUGO, Gior. ital. dermat. e syph. **66**:1120 (June) 1925.

Felugo uses a 10 per cent. solution of calcium bromid in normal salt solution, injecting 1 or 2 gm. of the drug every day or every other day. Very good results are reported in itching dermatosis, especially in prurigo.

ACUTE SYPHILITIC MENINGITIS IN EARLY SYPHILIS. G. MILANI, Riforma med. **41**:701 (July 27) 1925.

The author reports a severe case of acute meningitis during early secondary syphilis. The patient had a macular rash on the chest.

PARDO-CASTELLO, Havana.

TRACHEO-ESOPHAGEAL PERFORATION. B. WISKOVSKI, Ceska dermat. **6**:1, 1924.

A man, aged 46, who had syphilis and who had not been treated, suffered from a cough without dyspneic symptoms for several months. He suddenly developed dysphagia. Swallowing of food resulted in coughing and vomiting. Esophagoscopic examination showed an extensive ulcerating gumma on the anterior wall, and two weeks later a tracheo-esophageal ulcer 6 cm. long and 3 cm. wide. The Wassermann test was positive. There was involvement of the liver and aorta. In spite of intensive treatment and gastrostomy, the patient died of pulmonary complications. Postmortem examination verified the clinical findings. The trachea was probably the primary site of the gumma, as the ulceration spread from the lower edge of the lesion along the left tracheal wall and not toward the esophagus.

MONILETHRIX. VLASTA RIHOVA, Ceska dermat. **6**:8, 1924.

This is the first case ever published in Czechoslovakia. It was unusual in that it was not hereditary, first appearing in a woman of *32* without any known cause. There was an absence of follicular keratosis or lichen pilaris on the extremities. The affection was limited to a small partially bald area in the left parietal region. Only the proximal portion of the hair was involved, the ends being of normal appearance.

A CONTRIBUTION TO THE ETIOLOGY OF CHRONIC ECZEMA. LJUBIMKA MAXIMCENA, Ceska dermat. **6**:15, 1924.

There are certain dermatoses which resemble clinically a chronic eczema or eczema chronicum circumscriptum, and which by their localization, configuration and clinical course may suggest a mycotic origin. They are usually resistant to the routine treatment for chronic eczema. In a certain percentage of these cases it was found that intradermal administration of the trichophytin gave positive results. Furthermore, the results of the use of tar—a well known antimycotic specific—confirmed the suspected etiology. It would, therefore, seem advisable to keep in mind the possibility of trichophytic origin in cases of chronic eczema even if the mycotic nature of the affection is not manifest.

SIGNIFICANCE OF THE DIASTATIC POWER OF THE BODY FLUIDS IN EDEMA. NETOUSEK, Ceska dermat. **6**:33, 1924.

The author obtained negative results on examining a transudate (from edematous legs) from the standpoint of its diastatic power, by the modified method of Wohlgemuth. But when he analyzed by the same method the content of vesicles from a case of dermatitis herpetiformis Duhring, he obtained positive results, which shows that the nature of the two liquids is different as is in all probability their biologic formation.

LEUKODERMA FOLLOWING HERPES TONSURANS MACULOSQUAMOSUS. J. CRHA, Ceska dermat. **6**:34, 1924.

To the two previously reported cases the author adds four more in patients with deeply pigmented skin, and advances the following theory: Just as in syphilis the toxins of the spirochete may injure the function of pigment-forming cells, it is possible that other toxins may do so—either *Trichophyton tonsurans* or some unknown microbe causing pityriasis rosea Gibert. In all reported cases the pigment-forming cells were in a state of heightened activity prior to the onset of pityriasis: three patients were sunburned, one had deep racial pigmentation. Hyperfunctioning cells are especially sensitive, and an agent that would otherwise have no effect may paralyze their activity, with resulting leukoderma.

RADIUM IN TREATMENT OF LUPUS VULGARIS. F. V. NOVAK, Ceska dermat. **6**:57, 1924.

Four hundred patients were treated by radium emanation. The author describes his flat applicator, its use and clinical results. His applicator consists of a flat glass ampule, 0.3-0.5 mm. thick. It is filled with radium emanation and applied directly to the lesion. In this manner the bactericidal properties of beta rays are used, and an inflammatory reaction is brought on that is followed by a rapid resolution. The resulting scar is white and soft. Remaining or recurring single lupus tubercles are treated by radiopuncture.

BISMUTH IN THE TREATMENT OF CHRONIC SYPHILITIC ENDARTERITIS. JIRI SERF, Ceska dermat. **6**:75, 1924.

Treatment with a compound of iodin, bismuth and quinin gives excellent results in cases of syphilis of the aorta and aneurysm. The treatment consists of two series (from four to six weeks apart) of twelve deep intramuscular injections of 3 c.c. each, twice a week. The injections are painless and well tolerated. Improvement in symptoms and the Wassermann reaction is rapid. A weak myocardium, slight hypertension and marked hypertension, are contraindications.

AUTOHEMOTHERAPY. Salsa, Ceska dermat. **6**:89, 1925.

The author relates his experiences with injections of the patient's own serum, a form of unspecific desenstizing therapy first introduced by Ravaut. It is especially beneficial in tuberculosis and hydrosadenitis. Used in the early stages of herpes zoster, it seems to arrest the progress of the disease and to prevent necrosis. It is also recommended for urticaria, senile pruritus, acute eczema and prurigo. It promptly controls the itching. The technic is simple and inexpensive.

ATROPHODERMA AND SCLERODERMA. F. KOGOJ, Ceska dermat. **6**:113, 1925.

After a thorough review of previous literature and study of his own cases, the author concludes that skin atrophies and sclerodermas depend etiologically on disturbances of internal secretions accompanied in many cases by some disturbance of the autonomous nervous system. Irritating substances are thereby formed in the body, which are carried by the blood to the skin, and which cause pathologic changes. The latter differ in the two conditions. The atrophy producing agent causes a rapid toxic reaction. It affects not only the elastin but primarily—although often more slowly—the collagen. Elastin and collagen disappear, and the resulting space becomes trabeculated and filled by fat. The fatty islands—which the author also found in the subpapillary layer in considerable numbers also in acrodermatitis—invariably lie around sebaceous glands and hair follicles, which remain unaffected, judging from stained sections. The atrophying process spreads from these structures in a centrifugal fashion.

In discussing the question whether atrophy follows the inflammation in dermatitis atrophicus, the author believes the sequence is one of time only and not of any causal relation. The inflammation and atrophy are independent of each other. The irritating agent in scleroderma causes little protective, reactive inflammation; it masks its damaging effect at first by primary "nutritive" changes. The proliferation, however, soon changes into sclerotization without much actual hypertrophy or hyperplasia. The paper gives in detail the macroscopic and microscopic pathology of all forms of atrophies and sclerodermas.

The reactive faculty of normal, atrophic and sclerotic skin to applications of carbon dioxid is also discussed. The atrophic skin reacts much more intensely and extensively than the normal skin. The reaction of the sclerodermic skin is, on the contrary, far less pronounced and slower. The reactions then correspond with the pathologic changes in the two conditions.

ANGIOLUPOID BROCK-PAUTRIER. KAREL GAMALOSWSKI, Ceska dermat. **6**:173, 1925.

A woman, aged 34, with a family and personal history of tuberculosis for four months, presented a typical angiolupoid lesion on the side of the nose.

The lesion was 7 by 4 mm., brownish and of a soft, pasty consistency. The surface showed numerous enlarged capillaries. There were no lupous macules on pressure. The lesion was removed by radical operation with good result. Animal tissue inoculation gave negative results. Biopsy showed a slight cutaneous atrophy and diffuse infiltration of the reticular position of the derma. The infiltrate consisted of lymphocytes with scattered epitheliod and giant cells In the periphery of the lesion and in the deepest parts these epitheliod cells were more closely packed, but there was no typical, "ifiltration en nodules et en nappe," as described in classical cases. No tubercle bacilli were found. The case is an early one and would correspond to the second stage of Beech's sarcoid as classified by Kyrle.

Replying to the remarks of Pautrier, Levy, Salmon and Masson, which appeared in this bulletin six months previously, Darier upholds his conception of dyskeratosis and the dyskeratoses.

SPINKA, St. Louis.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

SULPHARSPHENAMIN. I. VALUE IN ACQUIRED SYPHILIS. J. C. FOX, Am. J. Syph. **9**:436 (July) 1925.

Fox gave sulpharsphenamin intramuscularly or subcutaneously in doses as high as 0.6 gm. without causing a significant local reaction, except in an occasional case, provided a solution of 33 per cent. concentration was used. The intramuscular or subcutaneous administration of the drug in patients in the secondary stage produced a slower healing effect on cutaneous and mucous lesions than is usually obtained with the other arsphenamins given intravenously. However, the end-results, as judged by absence of clinical recurrence and effect on serology, compare favorably with those produced by the other arsenicals. No superiority was shown for the drug in the treatment of patient with neurosyphilis, either when administered in the first instance or when given to patients known to be resistant to the other forms of treatment. Evidence was not obtained that the drug possesed particular value in reversing the serology of the Wassermann fast cases or in influencing favorably the clinical course of patients with disease of the cardiovascular system. The drug was found useful in treating three patients who had previously developed "shock" or "nitritoid" reactions after intravenous injections of the other arsphenamins. The route of administration seemed to play little or no part in determining the therapeutic effect, but was found to be of considerable importance as far as systemic toxic reactions were concerned. In this connection intramuscular injection was found to be the method of choice. Dermatitis was found to have a relatively high incidence, showing a total of six cases in 678 injections. It is important that three of these occurred among the 110 injections administered intravenously as compared with only one among 302 given intramuscularly. One patient, previously known to be intolerant to the other arsenicals, developed a severe grade of anemia of an aplastic type, but without purpura, following one course of seven subcutaneous treatments of 0.4 gm. each.

SULPHARSPHENAMIN. II. VALUE IN CONGENITAL SYPHILIS. E. C. DUNHAM, Am. J. Syph. **9**:463 (July) 1925.

Dunham finds that sulpharsphenamin is a drug which has a distinct place in the treatment of congenital syphilis. It seems to be as effective an agent as neo-arsphenamin. There is a great advantage to the pediatrician in having at hand a form of arsenic which can be prepared easily and injected subcutaneously. It can be used in high concentration and local and general reactions need not be dreaded.

NONINFECTIVITY OF BLOOD IN TERTIARY SYPHILIS. W. L. MCNAMARA, Am. J. Syph. **9**:470 (July) 1925.

Ten nonsyphilitic cases were transfused by McNamara from six syphilitic donors in the late stage of the disease. Four patients received one transfusion each, three received two, and three received three transfusions. One patient received blood from three donors. There was a marked improvement over the previous anemic condition in all cases. None of the recipients developed clinical evidence of syphilis or a positive Wassermann reaction during a period of observation of from sixteen to twenty-six weeks. From observations made on these cases and several others of which no accurate clinical record could be kept, McNamara concludes that it is ordinarily safe to use the blood of tertiary syphilitics for transfusion.

NEUROSYPHILIS. V. COMPARISON OF ARSENIC IN SPINAL FLUID FOLLOWING ADMINISTRATION OF SILVER ARSPHENAMINIZED SERUM. L. H. CORNWALL and C. N. MYERS, Am. J. Syph. **9**:485 (July) 1925.

Six determinations of the arsenic content of the spinal fluid were made by Cornwall and Myers in a case of general paresis. On four occasions these determinations followed, at intervals of from six to thirteen days, the direct administration of arsphenamin to the spinal fluid. The arsenic averaged 16.77 mg. per hundred grams. On two occasions the administration followed, at intervals of from four to eight days, the administrations of arsphenamin in auto-arsphenaminized serum. No arsenic was present in one of these examinations and in the other the quantity was too small to be quantitatively determined but was detected qualitatively and, therefore, recorded as a trace.

STUDIES IN SYPHILIS. XVII. PENETRATION OF ARSENIC INTO SPINAL FLUID AFTER INTRAVENOUS INJECTIONS OF TRYPARSAMIDE. J. A. FORDYCE and C. N. MYERS, Am. J. Syph. **9**:490 (July) 1925.

Examination made by Fordyce and Myers of the spinal fluids from patients receiving the routine type of treatment with intravenous injections of tryparsamide showed that in this group 14 per cent. showed the absence of arsenic. The amounts of arsenic found do not exceed those found by other methods of administration. In order to obtain these results, it is necessary to introduce seven and one-half times as much drug as in other cases. In other words, the dosage is extremely large as compared with other drugs. Due to the rapid excretion of tryparsamide, the amount of arsenic available for penetration is extremely small after the twenty-four hour period. Experimentally, examination of the brain shows that nine times the arsenic concentration is maintained in the brain after silver arsphenamin with the use of one-fifteenth the amount of arsenic injected. It is shown that tryparsamide does not possess an unusual power of arsenic penetration into the central nervous system. Therapeutic penetration is hypothetical in that other factors which may enter into this condition are not available either experimentally or clinically.

BLOOD SERUM GLOBULIN IN LEPROSY. C. N. FRAZIER and H. WU, Am. J. Trop. Med. **5**:297 (July) 1925.

The results of the investigations made by Frazier and Wu indicate that Sia's globulin precipitation test is positive in certain cases of leprosy, particularly in the nodular and mixed types of the disease. Of the thirty-two cases of leprosy in which this test was made, seventeen were positive. In all these cases the percentage of blood serum globulin was estimated. The nodular cases showed an average of 4.68 per cent.; the mixed cases, 4.52 per cent.; the active maculo-anesthetic cases, 4.23 per cent. and the latent maculo-anesthetic cases an average of 3.11 per cent. It was impossible to see any relationship between the serum globulin content of the blood of the cases treated with the ethyl esters of chaulmoogra oil, and those not treated, sufficient to make it of any value as a clinical test for determining the efficacy of such treatment. It is suggested, however, that the blood serum globulin and the precipitation test be studied in this relation to ascertain whether or not there is any decrease in the amount of serum globulin or the positiveness of the test parallel with clinical improvement. Apparently the serum globulin in long standing cases, in which the infection has become clinically latent, does decrease to a point within its normal range. This has been true of the malculo-anesthetic cases in this series which have never had any form of treatment, and suggests the close relationship of activity of infection and serum globulin content in leprosy.

REGRESSION OF JENSEN RAT SARCOMA. W. H. WOGLOM, J. Cancer Res. **9**:171 (June) 1925.

Woglom states that comparison of the curves for growing and receding Jensen rat sarcomas shows that the latter fall behind in proliferative energy at about the tenth day. Spontaneous cure seems to be accomplished by the immunity which this sarcoma engenders in its host. Bilateral Jensen sarcomas of the same age pursue a similar course; either both grow or both recede. A knowledge of this fact permits investigation of the early phases of regression. Tumors which are to recede are attacked first at the periphery by some deleterious principle, or condition, associated with the connective tissue of the host. As a consequence, a zone of necrobiosis, followed by what appears to be a secondary fibrosis, sweeps inward from the margin and the neoplasm is thus gradually converted into a fibrous nodule.

BEHAVIOR OF COAL TAR IN ADULT AND EMBRYONIC TISSUE. L. H. JORSTAD, J. Cancer Res. **9**:232 (June) 1925.

The problem investigated by Jorstad was: How does coal tar produce cancer? It is shown that the primary changes are a movement of fixed tissue cells toward the drops of viscid tar. The tar does not act to stimulate growth but to attract cells to it and away from their blood supply. Growth is a secondary phenomenon which intercedes only when the cells become sufficiently reduced by a pulling away of the endothelial cells of adjacent capillaries. The coal tar acts to attract cells only in that it dissolves the ergusia of the cells. Its action continues until it becomes saturated with this substance. It may then be inactive in the tissue or if conditions are suitable it may migrate into veins which contain little of the ergusia, as any substance containing a surface tension lowering substance may migrate from points in the medium containing a high concentration of the surface tension lowering substance to points of lower concentration of this substance. In the sparsely cellular connective tissue of

adults it is very difficult to collect together sufficient cells to produce growth. In the more cellular mesenchyme of embryos more densely cellular masses are easily brought together as they are easily produced in the more cellular epithelial structure of both adults and embryos. This failure to pull cells from the sparsely cellular tissue of adults is not due entirely to the few cells present but to the fact that they become exhausted of their ergusia and degenerate. In a few animals densely cellular masses were accumulated by drops of tar. Tar becomes toxic for the whole animal and leads to cachexia through its ability to thus draw the ergusia to it.

PREOPERATIVE SKIN DISINFECTANT — ALCOHOL-ACETONE-AQUEOUS SOLUTION OF MERCUROCHROME. W. W. SCOTT and J. H. HILL, J. Urol. **14**:135 (Aug.) 1925.

The alcohol-acetone-aqueous solution of mercurochrome-220 soluble, made by dissolving 2 gm. mercurochrome in 35 c.c. of distilled water and then adding 55 c.c. of 95 per cent. alcohol and 10 c.c. of acetone, is recommended by Scott and Hill as a very efficient preoperative skin disinfectant. Better skin sterilization is obtained with it than with iodin, potassium mercuric iodid and picric acid. Its application is accompanied by no pain and is, therefore, of special value in operations done under local anesthesia. Regardless of the age of the patient or location of the operative field, no instances of dermatitis have occurred following its use. The solution penetrates more deeply than iodin and potassium mercuric iodid. It penetrates at least as deeply as picric acid and seems to be a little more uniformly distributed at its lower level of penetration. It retains its high bactericidal properties at least forty-six days. It has a relatively low toxicity. The color of the preparation is such that there can be no doubt as to the extent and thorough preparation of the operative field. It should not be objectionable on account of its stain because the solution completely dries on skin in less than two minutes. Any stains accidently obtained are readily removed by surgical solution of chlorinated soda.

TREATMENT FOR WARTS OF FOOT. J. MARKEY, U. S. Nav. M. Bull. **23**:141 (Aug.) 1925.

The form of treatment which Markey has found most effective in all cases was modified from that of various authors. It is local only. The foot is thoroughly cleansed with green soap and water. The area of the ball of the foot surrounding the nodosity is painted with collodion (to protect the normal epidermis from the continued action of drugs). The thickened epidermis is cauterized with fuming nitric acid or strong solution of caustic potash. When a hole which approaches the diameter of the callosity has been eaten away to a depth at which the patient first complains of pain, it is filled with a 15 to 20 per cent. salicylic acid ointment. A felt corn plaster of nearly 3 inches diameter, having an aperture of half an inch, is then taped over the treated area. An additional reservoir of ointment is placed in the opening of the plaster if the foot is to receive only one dressing a day. Each morning the entire dressing is removed. The loose detritus and dead tissue are gently scraped away and the ointment is applied as before. The ordinary case will require only six or seven applications of this type, whereas in obstinate cases the treatment may have to be continued for a fortnight or longer. The lesions are prone to recur if treatment is not persisted in until the last vestige of the papilloma is removed.

Case of Fusospirillary Infection Which Developed During Active Arsphenamin Treatment. J. A. Hillsman and T. L. Driscoll, Virginia M. Month. **52**:312 (Aug.) 1925.

Hillsman and Driscoll report a case of Vincent's angina developing the day following the third injection of arsphenamin in as many weeks which they say does not speak well for intravenous medication as a cure for the disease. Local cleansing, followed by application of neo-arsphenamin, did not bring about any change for the better in this case, and, further, brings suspicion on arsphenamin as a cure for Vincent's angina, either locally or intravenously. Rapid improvement of this case coincident with the intravenous use of tartar emetic seems to point to the efficacy of this treatment.

Blood and Tissue Changes in Cancer. J. A. Shaw-MacKenzie, J. Trop. Med. & Hyg. **28**:297 (Aug. 15) 1925.

By means of serum reactions or blood tests, Shaw-MacKenzie has been able, without any clinical knowledge of a case, to differentiate cancer from non-cancerous lesions in the majority of cases and, what is hardly less important, in obscure cases and after operation to exclude the presence of cancer. Up to the present, in a total of 261 serums examined (including cancerous, non-cancerous and normal), the method has proved correct in 248, or 95.3 per cent. The errors have been associated chiefly with tuberculous, sarcomatous and febrile conditions. In one case (obscure abdominal) the reaction was "negative," but two months later, on postmortem and microscopic evidence, a primary carcinoma of the liver was found. So far, twelve cases of cancer of the stomach have been successfully differentiated from five cases of gastric ulcer, the diagnosis having been verified later. In one case, among others, the serum reactions were found to be quite normal in a patient nine years after removal of her breast for scirrhus. On the other hand, it has been possible to decide as to the latency of the disease after operation. In two cases Shaw-MacKenzie found the "positive" reaction present twelve and eighteen months, respectively, after previous removal of the breast for scirrhus. The patients looked well and were apparently in good health, but within three months of that finding metastasis was only too evident in each case. In another case the reaction was present previous to a small local recurrence after operation for squamous epithelioma of the skin, some twelve months before. These cases show that as long as the reaction persists, the patient cannot be considered free of the disease. It is not claimed that the reaction is specific. There is 5 per cent. margin of error, but the practical utility of the reaction is not greatly affected and is evident in 95 per cent. proving correct.

Congenital Syphilis and Pregnancy. Récamier, Ann. de mal. vén. **20**:515 (July) 1925.

Récamier treated four women, aged from 20 to 28 years, who first presented signs of syphilitic infection after the birth of the first baby. None of the women had an abortion, and the infants were normal. Investigation revealed that the fathers of the four women had a history of syphilis. The pregnancy seemed to have awakened the latent congenital syphilis. The efficiency of the specific treatment confirmed the diagnosis.

Sweating in Infants. A. B. Marfan, La Clin. Pediat. **7**:321 (June) 1925.

Marfan urges the necessity for guarding infants against sweating, as this invites suppurative skin affections and perpetuates them. Artificial feeding and rickets are responsible for excessive sweating, and the main indications

in pyodermatitis is a change to breast feeding and means to combat the rickets. Local measures are futile unless the tendency to excessive sweating can be overcome.

HERPES ZOSTER WITH SYPHILIS. M. ARTOM, Gior. ital. di derm. e sif. **66**:1044 (June) 1925.

Artom describes two cases in which herpes zoster developed in the course of neurosyphilis; another two in tabes, and two in general paresis. The onset always corresponds with a flaring up of the syphilitic process. One tabetic had herpes zoster on the chest when gastric crises first developed, and had another attack, two years later. The zoster was restricted to the neck this time, as symptoms of cerebral syphilis became manifest.

EXTRAGENITAL PRIMARY CHANCRES. F. RONCHESE, Gior. ital. di derm. e sif. **66**:1123 (June) 1925.

Ronchese found multiple chancres in 156, that is, in 7.4 per cent. of his 1,132 cases of initial syphilis. The primary lesion was extragenital in ninety-four cases (thirty-three men).

DERMAL LEISHMANIASIS. E. RABELLO, Ann. Brasil. de dermat. et syph. **1**:3 (Jan.) 1925.

Rabello gives illustrations showing the mutilating effect of leishmaniasis affecting the skin and mucous membranes at the present day and as depicted in prehistoric pottery in Peru. He protests against its being called American leishmaniasis, as he declares that it is the same affection known elsewhere as Oriental sore. Any difference in aspect and course is due to the secondary infections. Fully 90 per cent. of the cases in Brazil are mild, and spontaneous cures are common. The 10 per cent. of grave cases does not justify geographical limitations.

XANTHOMATOUS GIANT CELL TUMORS. O. WUSTMANN, Deutsch. Ztschr. f. chir. **192**:381 (Aug.) 1925.

Wustmann believes that these pathologic products are not true tumors, and certainly not true sarcomas. They are formed to accumulate the excess of cholesterol in these patients. Xanthomatous new growths are strictly dependent on the cholesterol diathesis. They practically never metastasize, and their growth is not infiltrative and destructive.

MALARIA TREATMENT FOR GENERAL PARALYSIS. JAGIĆ and SPENGLER, Wien. klin. Wchnschr. **38**:859 (July 30) 1925.

Jagić and Spengler state that patients with a syphilitic mesaortitis suffer no ill effects from the malaria treatment. In most cases they observed a considerable decrease in the blood pressure, and in patients who had symptoms of angina pectoris the symptoms were not infrequently relieved.

SYPHILITIC NEPHRITIS. H. BURGERHOUT, Zentralbl. f. inn. Med. **46**:834 (Sept. 5) 1925.

When in the course of syphilis a nephritis is observed, it is hardly possible to prove that the latter is caused by the syphilitic infection. Burgerhout believes that in cases in which the syphilitic infection undoubtedly preceded the nephritis, and which are characterized by high albumin content, reduced secretion of urine, normal and low blood pressure, and the absence of red cells in the urine indicating a tubular affection (nephrosis), we are justified in diagnosing the disease as syphilitic nephritis. Specific treatment may or may not be successful.

Society Transactions

AMERICAN DERMATOLOGICAL ASSOCIATION

Annual Meeting, May 4, 1925

INFORMAL ROUND TABLE DISCUSSION ON DERMATOLOGIC THERAPEUTICS

TREATMENT OF DERMATITIS VENENATA WITH RHUS TOXICODENDRON.

THE PRESIDENT: It has been requested by Dr. Williams that we discuss the treatment of dermatitis venenata with *Rhus toxicodendron* tincture.

DR. WILLIAMS: We are all familiar with the treatment of dermatitis venenata, and all have had excellent results. I think the *Rhus toxicodendron* preparation made from the ivy is in almost exclusive use in the eastern and middle portion of the country. Mr. Mulford tells me that on the west coast, where there is practically no sumac, and where the prevailing poisonous plant is *Rhus diversiloba,* the *Rhus venenata* preparation is used with success. I do not understand why the *Rhus venenata* antitoxin should work unless the two are identical. Last week a young woman came to my office who had a typical ivy poisoning, with intense itching and great swelling. The woman had been subject to ivy poisoning since youth, and she knew as well as I that it was ivy poisoning. She was a nurse in a hospital. She said she had received as an Easter gift a bracelet made of black lacquer, and the dermatitis was located where the bracelet had been pushed up and down on her arm. The next day the eruption began to develop. Within a week she had a full blown case. We are all acquainted with the dermatitis from lacquer. I had no lacquer antitoxin, but the next day I gave her an injection of *Rhus toxicodendron* in the buttocks. The next day there was some decrease, but she was given another injection in the deltoid. By Saturday she was well enough to go to the matinee, and by the next week she had completely recovered.

DR. SCHAMBERG: I have not treated patients who had lacquer poisoning, but I have had the impression that the *Rhus toxicodendron,* particularly used internally as a prophylactic, acted against the light forms of *Rhus* poisons. Some patients will develop a dermatitis late in the fall, in October or even in the dead of winter, when we would not expect the ivy to be active, and those patients have been protected by the administration of *Rhus toxicodendron* by mouth. I think the advantage of the antigen is that at the beginning of an attack it acts more quickly by injection, but for purposes of prophylaxis the oral administration is superior. I have seen the injection produce a pronounced dermatis venenata at the site of injection, probably from an overdose for that particular person.

DR. WILLIAMS: The poison oak of the Pacific Coast is described by McNair as closely resembling poison ivy, and I would expect the *Rhus toxicodendron* to be effective in those cases.

DR. GOLDENBERG: I should like to ask Dr. Williams whether the nurse had received in addition to the antigen, local treatment before she came to him.

DR. WILLIAMS: She had used salves of all kinds as local treatment, which had no effect. She became steadily worse. I have never seen local treatment have any effect.

DR. WHITE: I expect to have patients back at work in a week under treatment with white lotion. I keep them quiet, and no matter how severe the bullous eruption may be they are usually well within a week. The white lotion is sopped on every half hour, and the affected part is never bandaged under any circumstances. Within two or three days the skin becomes stiff, white and dry and may even split open. Then the lotion is abandoned and Lassar's paste is applied and worn constantly until a soft, more or less normal skin develops. This requires three or four days more.

DR. MONTGOMERY: We use a paste made of salicylic acid, 2 per cent., zinc oxid and starch, 25 per cent. of each and glycerin. It is Lassar's paste, but employing glycerin instead of lard or cold cream. We use this regularly as our treatment of choice. We do not use it when the condition is becoming worse, for we do not wish to clamp back the effusion, which is Nature's way of throwing off the virus from the skin. If the eruption is receding, it does well.

DR. GEORGE HENRY FOX: The great difficulty in this disease is the uncertain course of the infection. In ivy poisoning there may be a severe eruption that will disappear in a day or two, while on the other hand some cases will persist for a week or two. Without some control I think it is difficult to estimate the value of any remedy.

DR. SCHAMBERG: I think we all encounter the average cases in which the patient gets well under average treatment in the course of a week or so; but we see the cases in which there is a constant tendency to progress in spite of anything, and it is in those cases that the progression immediately ceases if the antigen is used, and the patient gets well.

DR. SUTTON: I think many people are sensitized to *Rhus toxicodendron*. Farmers who work with the old, dry vines in winter often are attacked. We place great dependence on a saturated aqueous solution of aluminum acetate. I have not yet employed the antigen, but have had good results from the administration of small doses of the specific tincture, as suggested by Schamberg.

DR. COLE: May I ask how many have used the antigen?

DR. FORDYCE: I have used the antigen for two years and have been much impressed with the rapidity of its action. After two injections the eruption almost disappears, and three will usually cure the condition. I give daily injections.

DR. HIGHMAN: I wish to say a word in this connection. I had a patient recently whom I mentioned at the last meeting of the New York Dermatological Society. Sometimes ivy poisoning is one of the things that is not what it seems. A woman came into my office with a history of having been exposed to ivy poisoning. She had been out walking on a warm day and did not know poison ivy when she saw it, so she sat in some. The leaves were not out yet. In spite of exposure to *Rhus toxicodendron*, I asked her whether she had a primrose at home. She said she had not. I tried all methods of treatment I knew, but she did not get any better. A few days later she called

up and said a friend who was visiting her said, "What a beautiful primrose you have" On my advice, she threw out the primrose, and recovered promptly. It may be that some cases of "ivy poisoning" are due to other factors.

DR. E. L. OLIVER: I have been greatly impressed with the value of the antigen. I have used one injection, which I think starts these patients on the way to cure, and it is only in the very severe cases that I use a second injection. The condition in most patients clears up in two or three days after one injection, as against two or three weeks before we used the antigen.

DR. C. MORTON SMITH: A Greek fruit pedler came to the hospital with a typical case of ivy poisoning. He had not been out in the park he said, or anywhere except delivering fruit, largely peaches. On a windy day the leaves that he had over the peaches were blown away, and he found some nice green leaves by the roadside, and he gathered them and spread them over the fruit. They were the leaves of poison ivy. Some hitherto unknown sources of poison ivy poisoning may have had a similar origin.

DR. WEIDMAN: The uncertainty of the conditions under which we judge the effects of ivy poison therapy appeals to me, and accordingly we experimented on a series of University students in this connection. Last spring we plotted out their susceptibility by applying the virus to the arm. Then we gave them a "protective" injection (four injections into the buttock). Thereafter both the alcohol extract and the plant ivy (and in some of the students the antigen as a control) were applied to the arm. All of the students developed an ivy eruption at the site of application. The four intramuscular injections did not protect against ivy poisoning.

DR. WILLIAMS: The treatment of ivy poisoning with alcohol is good. It is exceedingly effective in the early stages. I never give the antigen in the ordinary mild cases with few vesicles. If there are just a few vesicles here and there, the patients all get well by cleansing with soap and water, but if there is a temperature of 101 or 102 F., and water is running out of the blisters, one cannot scrub them, and this would have no effect anyway. It is in these cases that usually run from two to four weeks that we see a cure within forty-eight hours with antigen.

DR. SCHAMBERG: If any of you have cases of suspected primrose dermatitis you may determine the etiology by an allergic test. We have on hand a solution of primrose and have on several occasions made a distinct wheal at the site of the inoculation. There is an allergic reaction when the patient is susceptible to primrose.

DR. HIGHMAN: I am gratified to be in a position to corroborate what Dr. Schamberg has just remarked about ivy poisoning and primrose. In one of my papers on eczema I reported this and found that on making an extract of the sepals we found an active antigen, but the most active antigen came from the fuzzy stem of the primrose.

DR. HOWARD FOX: I tried to have some fun this morning in my paper in regard to the "Primrose House," which is one of the well-known beauty parlors in New York. Their ignorance of dermatology is shown by their choice of a name. In their ridiculous circulars they give definite directions for "face moulding," and in one instance said, "We speak not in terms of dermatology but in terms of physiology."

DR. GUY: I have used the antigen in a number of cases, and I am impressed with the fact that it is efficacious in shortening the length of the attack in a certain group of cases. In the cases of two children with extensive

eruption which was spreading rapidly, the injection of 0.5 c.c. intramuscularly caused a marked increase in symptoms. It has occurred to me that perhaps some of the criticism is due to starting with too large a dose. On cutting down the dose, I could proceed without further trouble.

DR. COLE: I would like to agree with all the good things that have been said, and also agree with Dr. Guy in regard to dosage. We always start with 0.3 c.c., and then in two days give 0.5 c.c., and we rarely have to use more than the two doses.

DR. POLLITZER: I wish to question, in the interest of dermatologic science, the propriety of the use of the term "antigen" in this connection. An extract of the plant is not an antigen and does not work like an antigen.

DR. SCHAMBERG: I am not sure that the use of this preparation by mouth does not produce a substance that works like an antibody. If it promotes the development of an antibody it could be properly designated an antigen, but we have no definite proof of that as yet.

TREATMENT OF PRURITUS ANI.

DR. WALLHAUSER: Pruritus ani is probably one of the most troublesome conditions that we are called on to treat, and while the ascribed causative factors are many, and when found present should be considered, I would like the privilege of presenting a simple plan of treatment that has been successful in relieving the pruritus in all cases which have come under observation during a period of many years.

This plan consisted of applying an ointment of yellow mercuric oxid, 3 grains (0.19 gm.), petrolatum, 1 ounce (30 c.c.). This is applied mornings, preceded by bathing the affected areas with a 1 per cent. aqueous solution of sodium biborate. This was followed by applications of ointment of rose water at bedtime. Many patients have been treated including some with cases of long duration in which considerable thickening and infiltration of the skin with rhagades occurred, as well as three who had developed a marked kraurosis vulvae, one of which presented several areas of epitheliomatous proliferation. The rapidity of the relief of the pruritis in nearly all cases was marked.

In the great majority of cases no pathologic conditions other than the skin lesions were observed. In a few, however, hemorrhoids or vaginal discharges were present, those patients being advised as to further treatment for these conditions. Regarding the cases of kraurosis vulvae, the pruritus was relieved in two, but the patients failed to report for observation as to the final outcome concerning the effect on the patchy thickening. The third patient, who had presented several areas of epithelioma to which radium had been applied, made a complete recovery and was observed one year later, at which time there was no recurrence of the epithelioma, and the patient was entirely free from pruritus.

I am not unmindful of the complex nature of the problem of pruritus ani and offer the foregoing plan from a therapeutic standpoint only for the relief of the skin involvement, and hope that others will find it a useful addition to their armamentarium.

DR. MONTGOMERY: Years ago when I was at the old College of Physicians and Surgeons, now Columbia University, down on Twenty-third Street, New York, Dr. Sands one day spoke of the use of calomel ointment in this condition. That was the beginning for me of a number of fortunate cases. I think its mode of action lies in killing the streptococcus. It acts wonderfully. I used it for years, until one day Mr. Young, a druggist, told me that he had

thought that he was condemned to the enduring misery of a continuous pruritus ani until he employed an ointment I frequently prescribed, consisting of the red mercuric oxid, camphor and carbonate of lead. He had already employed the calomel ointment unsuccessfully. Since this experience this red mercuric oxid is my remedy of choice. The full mode of action seems to be that either the calomel or the red mercuric oxid in the warm alkaline salt (NaCl) solution of the blood serum or the mucous secretion is turned into mercuric chlorid, which is formed continuously in small quantities and is quickly turned into the albuminate of mercury. In passing from one state to the other, it is nascent and very active and poisons the streptococci which cause the pruritus. As it is formed in such a small quantity and is so quickly turned into the albuminate, it does no harm to the tissues, and does not burn or corrode. As Dr. Wallhauser said, it does not seem to matter what the anatomic source of the trouble is, it acts admirably. I find, however, that in many cases the pruritus recurs, which I attribute to a recurrence of the streptococcic infection. Repetition of the treatment quickly abates the nuisance.

Dr. Howard Fox: I should like to know whether any of you have been impressed with Montagne's book on the perineum. He says many cases are due to a misdirected sensation of itching. There may be something wrong with a certain viscus, and the sensation is misreferred, and the patient scratches the perineum.

Dr. Ketron: I have believed for a long time that one of the most important things in treating pruritus ani is to discontinue the use of toilet paper. I ask my patients to wash the anus, after each bowel movement, with a boric acid solution. After drying with absorbent cotton an application is immediately made of a 2 per cent. ammoniated mercury ointment or some similar preparation.

Dr. Montgomery: The ammoniate of mercury is the same as the calomel ointment, except that it acts more strongly, as the NH_3 seems to be hitched to the HgCl more loosely than the O and therefore mercuric chlorid is formed more quickly by the action of the warm alkaline sodium chlorid solution in the blood.

Dr. Shelmire: In the country in the introduction of his work, one of the foremost proctologists speaks of the difficulty in curing these conditions. He treated an Irishman. He met him on the street afterward, and the patient said that a woman told him to use some lard and calomel, and that cured him. That was reported about forty years ago.

Dr. Williams: I wish to say a word about the value of discontinuing the use of toilet paper and washing the anus, as Dr. Ketron brought out. This will relieve many cases of pruritus ani. There is great irritation from sticky feces, and if this can be eliminated by washing with soap and water and then drying carefully, these patients can be relieved promptly.

Treatment of Pemphigus.

Dr. Wende: Of the patients whose cases were reported by me last year one died; eleven recovered and have remained well. At the time I made the report I gave the history of the case to which reference has been made. The patient who died was a woman, aged 75. She apparently improved for a time, but later the disease became active, and not withstanding the fact that general treatment was continued, no benefit accrued. Since last year's report, we have had twelve other cases. Up to the present time, with the exception of two, all have recovered under the Davis treatment, and they have remained well.

DR. SCHAMBERG: I wish to say that I have employed this treatment in several cases of pemphigus, particularly stimulated by the report of Dr. Wende at the last meeting, and that it has absolutely failed. One was a beginning case in a young woman and was limited to the mouth and lips. She received thirty-four injections alternately of the iron and coagulen, without any result. Several other patients were treated without result. The patient to whom I have just referred promptly recovered under the intravenous administration of mercurochrome-220 soluble. This was brought to our attention by one of my associates, Dr. Greenbaum, who had an almost immediate effect in an extensive case of pemphigus when the patient looked as if he would die. He was covered with blebs, and on the injection of 5 mg. per kilogram of body weight, there was a miraculous clearing up, but he had a relapse. I think I would be persuaded to use mercurochrome in 5 c.c. of a 1 per cent. solution, running up to not more than 20 c.c. I also wish to state in this connection that I have seen several cases in which there were raised plaques in the mouth with a pseudopedicle, lasting for two years in one case, with bleeding crusts over the lips, and that patient's condition cleared up under the intravenous use of mercurochrome. The obstetricians and gynecologists give as a routine 5 mg. per kilogram, which represents about 30 c.c. for the average person, but I think in the early cases one should not take that risk. I believe that one is justified in giving up to 20 c.c.

DR. GOLDENBERG: I think at the last meeting Dr. Highman expressed some skepticism about our treatment of pemphigus, and he afterward drew my attention to the fact, just related by Dr. Schamberg, of getting results with mercurochrome. We tried this on one patient with pemphigus lesions in the mouth and of the skin, but I must say that the condition was not only not improved, but became considerably worse. We used 3 mg. per kilogram, and the woman was in a serious condition for several days. I think the lesions in the mouth were irritated considerably. I must confess, also, that I have seen nothing but failures from the treatment recommended by Dr. Wende.

DR. WENDE: I think Dr. Fox knows about the case which I saw in New York City. This case was one of the worst that I have seen this year. The man's whole body was denuded; his mouth was filled with blisters; some of the lesions were hemorrhagic; he could hardly move in bed, and his appearance seemed to indicate the beginning of the end. To my inquiry whether the Davis treatment had been tried, they said it had not. It was started immediately, with the result that the man got better. I received a letter three months later stating that he was back at work. It seems that Dr. Fordyce saw this patient still later in a fresh attack, which was fatal.

DR. GOLDENBERG: It is my experience that in all cases of pemphigus the patient may improve a little under the various methods of treatment used for this disease, but all cases end fatally.

DR. ORMSBY: I was much impressed with Dr. Wende's remarks. I have used the treatment in three cases. In one severe case the patient had generalized lesions of pemphigus, including involvement of the mouth. A bad prognosis was given the family of this patient. We gave the treatment according to the Davis method, and for four weeks there was no change. Then in about two months he apparently recovered. We presented him at the annual meeting of the Chicago Dermatological Society in January, and recovery seemed to have occurred. The patient then went to California and remained for several weeks. On his return journey the disease recurred, and at the present time he is in a desperate condition. (NOTE: This patient later succumbed.)

A patient with pemphigus vegetans improved wonderfully for about a month, then had a relapse and died in about a week. In a case of pemphigus foliaceus, great improvement occurred under this treatment, and the patient is in fair condition after ten months' observation and treatment.

DR. WILE: I have had several conversations with Dr. Wende, and saw a case with him and Dr. Cole. My experience is limited to ten cases of pemphigus. All the patients were hospitalized, and one was under my care for about seven months. In none of these cases were we able to stave off the inevitable end of the disease. At one time I had a letter from Dr. Greenbaum asking me to use mercurochrome in the dosage he recommended. It so happened that we had two patients with severe pemphigus in the ward who had failed to respond to the Davis treatment. We tried the treatment outlined by Dr. Greenbaum, and it had no effect. I wonder whether we are seeing the cases later. I think mine come in later than Dr. Wende sees them. Some of the patients have been treated for a long time, are in extremis and die within a week's time. In several cases we were able to give the treatment prescribed by Dr. Davis and as amended subsequently by Dr. Wende, of giving the remedy intravenously, but thus far I have not had a patient with pemphigus get well. I am hopeful that Dr. Wende's experience will be corroborated if we continue the treatment, and that we shall see patients get well.

DR. COLE: Last year we had four cases, and one of them was seen by Dr. Wile and Dr. Wende. In two of the cases the patients have seemed to get better, but in each case it has been the same story. In one case in which we used mercurochrome the patient was well for five or six months. Then her physician called me up and asked what to do. I told them I did not know of anything further, and they told me later they had gone to New York to get a good physician. I do not know whether she consulted one of our colleagues in New York or not.

DR. GUY: Of four patients treated by the Davis method, three are dead. The fourth one is living, and the disease is of six years' duration. I realize that this is a long time for a patient with pemphigus to live. She received the Davis treatment according to directions. During the entire course of the treatment she was never free from the lesions. She was then given 30 c.c. of 0.5 per cent. mercurochrome, and within forty-eight hours after the administration she had no new lesions. In two months she had a recurrence; the lesions involved the eyes. She is extremely emaciated. Now mercurochrome has no effect, but in some cases there is no doubt that it is of great service.

DR. GILCHRIST: Dr. Young says that we must use large doses of mercurochrome to get results. In one case we tried vaccine, and it did no good. The patient was put in a continuous bath up to the neck and was much improved, but the lesions on the face were as severe as ever. This man was under observation for fifteen years, then an enterologist gave him injections of sulphoichthyolate preparation, and he was well for eighteen months or two years. In a severe case of a girl of 18 I gave blood injections, obtaining the blood from relatives, and after one injection her condition cleared up, and she left the hospital. She had a relapse, and then we obtained relief by keeping her in a bath of linseed oil. This is soothing, but it did not cure the patient. Then I tried the serum from this case in the eye of a rabbit. An irritation of the eye resulted, but there was not another blister; I could not try the experiment any further, for in the meantime the patient had died. Dr. Fordyce

has said that there are curable cases of pemphigus and incurable cases, no matter what is used. When we are dealing with varieties of pemphigus it seems to me to be a fact that some are fatal and some patients seem to get well under the various remedies, and I presume this will be true until we find the cause of the disease.

DR. MCEWEN: I recently had contact with a case of pemphigus which was most interesting, particularly as to the manner and cause of death. The woman, who had been in poor health for a number of years, suddenly presented an acute outburst of bullae over the arms, trunk, thighs and face, with marked involvement of the conjunctivae, the mouth and the nares, and with a rise in temperature of several degrees and a rapid pulse. She was desperately sick. The Davis treatment was instituted at once, and the improvement in the skin in a week was remarkable. We felt that this improvement was due to the coagulen rather than to the iron cacodylate. After a brief period of improvement she began to run a temperature of 103 F. and more, with a gradually increasing respiratory rate. Although carefully searched for, a satisfactory explanation for these adverse changes was not at first apparent. The temperature finally reached 106.4 F. per rectum, with respirations 50, and it became evident that she was a victim of encephalitis. She developed the parkinsonian syndrome with lethargy, the pulse rate dropped to 85 to 90. Death was somewhat unexpected, and was apparently due to paralysis of the respiratory center. Had she lived one day more, we could have instituted the Mayo serum treatment and might possibly have saved her.

My deductions in the case were these: The dermatologic phases of pemphigus are symptoms only; the fundamental cause is cryptic infection, and it is possible that a number of organisms may serve as the exciting agent. Whether death occurs depends on the localization and the severity of action of the offending organism. The Davis treatment tends to clear the skin symptoms, but does not necessarily strike at the basic cause of the trouble.

DR. GILCHRIST: I think we have all noticed that when the skin lesions clear up it is a dangerous symptom. I think the organisms then get into the intestinal canal, and the patients die. In one case the temperature dropped from 103 to 94 F. following an injection of vaccine, and the eruption disappeared entirely.

DR. SUTTON: I think that the case Dr. Hazen mentioned yesterday was probably an instance of pemphigus chronicus with a superimposed bacillus pyocyaneus. I have found calcium chlorid, 10 gm. per day, in capsule, beneficial. It gives great relief from the cutaneous edema.

DR. FORDYCE: I should like to elaborate a little on the case to which Dr. Gilchrist referred and with which Dr. Wende is acquainted. The patient was a young girl who consulted me some years ago with lesions in the mouth. The Wassermann reaction repeatedly was negative. She later developed lesions on the body and then on the scalp. Clinically it was a typical case of pemphigus vegetans. Later, she went to Johns Hopkins Hospital and saw Dr. Barker, and he and Dr. Fels reported the case as pemphigus vegetans of long duration. She then went to Paris to see Dr. Darier, and said that there she received some injections of sea water and some topical remedies. I went to Paris in 1912, and the patient sent for me. She still had the outbreak on the skin. The next year I was again in Paris, and she came to see me. At that time she was entirely free from lesions and looked almost well. She has remained well. That was a case of what was clinically pemphigus vegetans, and it began in the mouth, as those cases often do.

DR. SWEITZER: I heard Dr. Davis' original paper and used the treatment in the first case of pemphigus I saw afterward. The patient was a man about 60 years of age, and I reported this last year. He remained well for about three years, but just before I left Minneapolis his physician told me that apparently he was at the point of death, having had a relapse. In a recent case in which I used the Davis treatment it was of no avail; then I used mercurochrome, and it had no effect. The patient died. I wish to call attention to the possibility of having a toxic mercury rash following the use of mercurochrome. I have had a number of patients in the hospital who had been given mercurochrome, and who have blossomed out with a red eruption and been desperately ill.

THE USE OF CRUDE COAL TAR.

DR. WHITE: I have had a great many letters from various parts of the country in regard to crude coal tar ointment. The real trouble has been that the various writers could not procure proper crude coal tar. We have the same difficulty unless we procure the substance from certain sources only. This difficulty means that this valuable drug is going to be lost unless this hindrance can be overcome.

Last year it occurred to me that we might improve the original formula by omiting the cornstarch and by mixing the crude coal tar with zinc oxid and then adding petrolatum only. I kept track of these cases for nine months, and found that 159 patients had been treated with this new preparation. On looking over the records, I found that sixty-four persons never came back, which reduced my cases to ninety-five. Concerning the ninety-five patients who were left, I came to the conclusions which I have published in *The Therapeutic and Dietetic Age*, which I do not believe any of you have ever seen. I thought I should like to have you know the improvement that has taken place, not only in the facility of making the ointment, but also in the results obtained. I will read these conclusions.

1. Crude coal tar combined in the proper proportions with zinc oxid and petrolatum and used in the strictly proper manner is to be recommended in moist and semimoist examples of infantile eczema, in semimoist cases of a subacute and chronic eczema in adults, in eczema seborrheicum of the hairy parts, in neurodermite of the scalp and of other parts of the body when the roentgen-rays are unobtainable, in moist, semimoist and macerated forms of epidermophytosis, in psoriasis of the scalp and in prurigo mitis.

2. In this series of cases of the diseases mentioned above the proper use of crude coal tar has resulted in approximately 61 per cent. of successes, 20 per cent. of improvements and in only 8 per cent. of failures.

3. This now advocated change, wherein the cornstarch is dropped from the older prescription and crude coal tar is combined only with zinc oxid and petrolatum, has essentially done away with the former pharmaceutical trials and difficulties, and at the same time has seemingly increased the therapeutic success of the drug.

4. The success of the new formula over the old is corroborated by several of my colleagues who have been asked to make this trial with me.

In using this crude coal tar I think we must remember these peculiar idiosyncrasies of the drug. The ointment must be used twice a day. The strength is one-half dram of the crude coal tar, one-half ounce of zinc and one-half ounce of petrolatum. This has proved better than the original ointment.

DR. SCHAMBERG: I think we are all convinced, particularly since our attention has been directed to this matter by Dr. White, that crude coal tar possesses great curative powers in some conditions. We have all been disappointed with variations in results. Two years ago I procured from a pharmacist in Philadelphia a crude coal tar that brought about excellent results, and it appeared that we had a panacea. After that all he furnished me had no result. Recently I had a conversation with one of our chemists, and the information which he gave me I think supplies us with a good clue as to the cause of the variations and failures. The pharmacist secured his coal tar from the wholesaler, the wholesaler secured it from the jobber or the coal tar plant, the jobber secured it from the people who make illuminating gas or make coke, and each batch is an entirely different product. That which is recommended by the French authors is only that obtained in the manufacture of illuminating gas. The Barrett Company in Philadelphia say that there is great variation in coal tar. They make a blend, and much depends on the size and character of the retorts and on the degree of heat applied in the distillation, and until this whole matter can be standardized, I think we shall continue to obtain varying results. There is something subtle in the crude coal tar, and someone must investigate the matter thoroughly and find out what it is that has these healing properties. I am hoping to obtain supplies soon from firms who have small retorts and know their product. There is much difference in the compound also, but there is great difference in the crude coal tar, and that depends on many manufacturers.

DR. MCGLASSON: I have had a great deal of experience with crude coal tar, not only in infantile eczema but in other types, particularly the weeping types of dermatitis. So far I have had no trouble with it. It is apparent that there is a difference in the coal tar in the different towns. My friends in Houston, Galveston and Dallas have complained of not obtaining satisfactory preparations, while we in San Antonio have had no trouble. Evidently it is not thoroughly washed, or there is some chemical irritant in the coal tar that causes the trouble. I have never had any fear of its use in large areas, and have used it many times with satisfactory results and no untoward symptoms. In eczematoid ringworm I find it advantageous, especially in acute vesicular stages. After its use we can proceed with keratolytic applications.

I think Dr. White deserves commendation for his long study of coal tar and its application in dermatologic therapy.

DR. J. E. LANE: I infrequently find any susceptibility to crude coal tar, but occasionally I do see a case. One patient, after using a mild ointment, developed marked swelling of the arm from the elbow to the shoulder, with intense burning and itching. This was proved to be susceptibility to coal tar by the latter application of a minute amount to a small area. Such susceptibility is infrequent.

DR. HOWARD FOX: For some time in using the crude coal tar of Dr. White I have added 5 per cent. of white wax. This seems to make the preparation adhere better to the skin and lessens the "messiness." I should like to know whether Dr. White's new preparation is more adherent and less disagreeable.

DR. WHITE: I think there is not much difference in that way.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, May 5, 1925

FRED WISE, M.D., *Chairman*

GRANULOSIS RUBRA NASI. Presented by DR. LEVIN.

A. G., aged 13, a schoolboy, had had a red nose since birth. The lower part of the nose was congested, red, and showed pinhead-sized red papules and pinhead-sized drops of sweat. The redness was prominent, and when the small beads of perspiration were removed, they were almost immediately replaced by fresh droplets.

DISCUSSION

DR. BECHET: I have been impressed with the comparative rarity of this disease during the last five years. Previous to that time I had observed a number of cases.

LEUKEMID. Presented by DR. LEVIN.

H. E., a Turk, aged 49, married, complained of a persistent generalized pruritus, loss of strength and increased fatigue. Examination revealed numerous excoriations and scattered wheals. The lymph nodes all over the body were enlarged, and the spleen was palpable below the free border of the ribs. The blood count revealed a leukocytosis of more than 21,000 and a lymphocytosis of 84 per cent.

DISCUSSION

DR. MALONEY: I agree with the diagnosis.

DR. NATHAN ROSENTHAL: This case belongs to the group of the so-called aleukemic leukemias, now called leukopenic leukemia because of the absence of leukocytosis and the presence of a differential blood picture typical of leukemia. It was rather peculiar that there was only a relative increase of lymphocytes, with only a slight adenopathy and a large spleen. The leukemid history extended over four years, but the leukemic history dated back only six months.

MAJOCCHI'S DISEASE. Presented by DR. LEVIN.

J. S., aged 41, married, had had the condition presented on his feet and face for four years, and on his forearm for seven months. The dorsum of both feet showed fresh purplish-red and livid macules, varying in size from that of a pea to that of a bean, and slightly elevated lesions, numerous telangiectasias, small areas of purpura and several large pea-sized annular lesions showing atrophy in the center and borders, which were made up of telangiectatic vessels. Both forearms on the extensor surfaces presented diffuse brown pigmented patches showing in their midst small atrophic areas and numerous small and large telangiectasias. Over the malar prominences, both cheeks were covered with small and large confluent brown macules.

MAJOCCHI'S DISEASE. Presented by DR. LEVIN.

J. B., aged 24, unmarried, born in this city, a stenographer, first noticed the condition on her legs ten years before. The other sites gradually became

affected, and recently the last lesion affected the back. Both legs showed diffuse lesions made up of cayenne-pepper-like spots, telangiectasias, annular lesions with atrophy in the center, purpuric spots and brownish pigmentation. The atrophy was most evident on the buttocks, especially the left, where, beside the other lesions, the atrophic spots had become confluent to form a large diffuse area of atrophy covered here and there with cayenne-pepper spots, telangiectasias and pigmentation. The interscapular region showed a livid patch about the size of a dime.

DISCUSSION ON MAJOCCHI'S DISEASE

DR. SCHEER: The eruption on the man is rather vague, and I cannot make a diagnosis. In the case of the girl, the condition is more definite; many of the lesions look like psoriasis, but one lesion about half an inch in diameter is typical of Majocchi's disease; it is annular, purpuric and has distinct atrophy in the center.

DR. LEVIN: I first saw the patient only a week ago, and he appeared then just as presented. On the dorsum of the feet are telangiectasias, purpuric and annular lesions; there is slight atrophy on the forearms and feet. I hesitate to make a diagnosis of Majocchi's disease, but the picture does not fit any other condition. I shall make a biopsy later.

The girl walked into the clinic a week ago, presenting livid and rose-colored macular and slightly elevated lesions which were hemorrhagic, telangiectatic, atrophic and showed marked atrophy over the buttocks; the case was immediately diagnosed as Majocchi's disease.

PITYRIASIS RUBRA PILARIS. Presented by DR. BECHET.

E. S., a girl, aged 21, from Dr. Whitehouse's service, said that the lesions had been present for nine months. On the dorsal surface of the fingers and hands the characteristic pale red acuminate papules were noted, some with horny formation at the central point pierced by broken hairs. The palms showed diffuse thickening. The acuminate papules were aggregated about the elbows, forming large, dry, red, roughened patches, with a branny desquamation on the surface.

BROMODERMA, RESEMBLING ERYTHEMA NODOSUM. Presented by DR. ROSTENBERG.

Mrs. A. L., aged 44, a Russian Jewess, was suffering from hypertension, for which she had been taking potassium iodid, phenobarbital, sodium bromid and nitroglycerin. During the last year she had had three attacks similar to the one presented, each one clearing up spontaneously in a few weeks. The last attack developed about a week before presentation, after she had taken a mixture containing about 6 grains (0.4 gm.) of sodium bromid to the dose, which she took for only a few days. On the external surface of each arm was an infiltration the size of a small orange, rather firm and painful to pressure; the cutis and subcutis seemed to be involved. The skin was dark reddish. On the right thigh was a similar but somewhat smaller lesion, and a small number of smaller infiltrations were scattered over various parts of the body.

DISCUSSION

DR. OCHS: I understand that the condition has recurred frequently. In that case I hesitate to agree with the diagnosis, for bromoderma does not disappear and then relapse.

DR. ROSTENBERG: The woman came to the Clinic on Friday, and my first impression was that the condition was an erythema nodosum of a rather unusual type; on going into the history of drugs, she denied taking anything excepting nitroglycerin. The day before, however, she admitted taking something which on investigation proved to contain bromid. She then stated that she had had three of these attacks during the past year, one of them so severe that she was taken to Lebanon Hospital, and the condition was there diagnosed as apparently being a bromid eruption. The distribution of the lesions spoke against erythema nodosum.

VACCINIA. Presented by DR. ABRAMOWITZ.

J. R., a 10 year old school-girl, from the Gouverneur Clinic, born in this country of Italian parents, was vaccinated three weeks before presentation, and showed a marked scar about 2 cm. in diameter. One week before the eruption first appeared on the hands without any premonitory symptoms. She presented confluent pustular lesions on the right side of the neck and chest and on the wrist and thighs; a few isolated lesions were present on the extremities, including the palms and soles. There were no lesions on her face or in the mouth, and she had no fever. There was no history of any drug being taken.

A CASE FOR DIAGNOSIS: DERMATITIS VEGETANS? Presented by DR. BECHET.

A. C., a girl, aged 12, from Dr. Whitehouse's service, stated that the lesion on her right cheek had been present for six weeks. Her mother, after the most careful questioning, stated that she had not given the child any internal medication, either before or after the appearance of the lesion. When she first appeared at the clinic the tumor-like lesion was moist, with an oozing granulating surface, resembling a granuloma pyogenicum; later it dried up and assumed a condylomaform appearance; it was raised and hard, with a verrucose-like surface. The child said it was painless. From its first appearance, which had changed considerably on the night of presentation, one might infer that it was a vegetating growth on a single or grouped pustular eruption, hence the tentative diagnosis of dermatitis vegetans.

DISCUSSION

DR. ROSTENBERG: Has the girl been taking bromid?

DR. BECHET: No.

DR. CHARGIN: The lesion has all the characteristics of broderma.

DR. ANDREWS: I agree with Dr. Chargin, but I believe the condition may be tuberculosis verrucosa cutis. I understood the patient to say that the lesion was of six months' duration. Bromoderma, however, seems the most probable diagnosis.

DR. BECHET: The mother denied having given the child any medication for nine months before or after having the lesion; she also stated that six months earlier the child's face was absolutely well. It was an interesting case. He had considered the diagnosis of bromoderma first, but with the negative history it was impossible to make that diagnosis. He had also considered dermatitis vegetans or a granuloma of some kind. He would make another effort to elicit something definite in reference to the ingestion of bromids, but the mother was so positive in assuring him that nothing had been taken internally that he did not anticipate much success in that regard.

CARCINOMA AND ACTIVE TERTIARY SYPHILIS. Presented by DR. LEVIN.

A. P., aged 48, an Italian shoemaker, had cut his right cheek about six months prior to presentation. This was followed by ulcers and a growth on the right side of the lips and right cheek. He presented a large, deep, dirty, irregular ulcer on the buccal surface of the right cheek. The right corner of the mouth and the upper and lower lips showed irregular and punched-out ulcers. The adjacent skin was affected. On palpation, a pigeon-egg-sized, hard, dense mass was felt in the affected area. The right anterior cervical nodes were palpable. The Wassermann test was four plus. The clean punched-out ulcers showed a tendency to heal after two injections of arsphenamin, but the rest were unaffected.

DISCUSSION

DR. MCCAFFERTY: If it proves to be carcinoma, surgical intervention should immediately be instituted, followed by radium or radiotherapy to the lymph nodes, which are frequently involved.

DR. ANDREWS: I should like to know what Dr. Levin proposed to do for the glands in this case.

DR. LEVIN: Good results in carcinoma of the mouth have been obtained with radium therapy. I hesitated to give this patient any antisyphilitic treatment, but I tried a small dose of arsphenamin, and the punched-out ulcers seem somewhat smaller. I shall not give more than two other injections. I expect to give deep roentgen-ray therapy for the glands of the neck.

A CASE FOR DIAGNOSIS, ANGIOMA SERPIGINOSUM? Presented by DR. FELDMAN.

A. E., a man, aged 23, unmarried, a clerk, about a year ago noticed a red discoloration on both sides of the face which spread to the dimensions presented. The patches were nearly symmetrical on the temples, the edges not sharply outlined, and areas of healthy skin could be seen within the affected lesions. There were many telangiectatic vessels present.

DISCUSSION

DR. SCHEER: I do not know what the condition is, but I do not think it is angioma serpiginosum.

DR. OCHS: Those who look at the case in daylight will not agree with Dr. Scheer, for the red-pepper spots are plain then and also the areas of healthy skin. In my opinion, any one examining the case in daylight would not hesitate about the diagnosis of angioma serpiginosum. When I saw the case a week ago, I made that diagnosis from that very fact, and spoke about the purple spots, the areas of true skin and the new blood vessel formation. It is difficult to see how any one could arrive at a different diagnosis.

DR. BECHET: About a year ago I presented a case before one of the dermatologic societies with a tentative diagnosis of angioma serpiginosum. The lesions in that case were similar to these, both in appearance and location. There were telangiectatic spots in annular formation with areas of clear skin between; they assumed a reticulated lacelike effect. Neither Dr. Wise nor any one else present at the time agreed with the tentative diagnosis. On further questioning, the patient stated that in his work he was constantly under a strong electric light, and it was the general opinion that the lesions were caused by exposure to this light, and that they were not angioma serpiginosum.

Dr. Feldman's patient was a linotype operator, and stated that he was constantly exposed to a strong light. In the uncertain light available this evening, I have not been able to observe any red-pepper spots, but in view of the history and the objective symptoms it is my opinion that this case is similar to my own and is actinic dermatitis and not angioma serpiginosum.

Dr. Feldman: The man is not intelligent enough to know that there were no signs of the disease a year ago; it started simultaneously on both sides and spread. He has been under observation for four weeks, and the part that developed later is more red and telangiectatic. Although some of the lesions are the cayenne-pepper spots. There are unquestionably areas of clear skin between the lesions. I regret that Dr. Scheer has not seen them, for they are distinct; there had even been some discussion as to whether it is normal skin or depigmented. From all that can be noted, it does not seem to be anything else. Lupus erythematosus has been suggested, but there is no evidence of that. The follicles are somewhat dilated, but not larger than those in the normal areas. I cannot assert positively that the condition is angioma serpiginosum, but that was the disease most nearly resembling it that he could think of.

Fixed Eruption from Bismuth. Presented by Dr. Levin.

A. B., a woman, married, having tertiary syphilis, had received several courses of arsenic and mercury. More recently she had been given several intramuscular injections of bismuth. Subsequent to the sixth injection, she began to complain of general aches and a persistent itchy eruption. Examination revealed several dime-sized to quarter-sized round, dark red and bluish red, slightly elevated and macular lesions. These faded slowly but were intensified by each subsequent injection.

Dermatitis Herpetiformis. Presented by Dr. Howard Fox.

J. T. M., aged 33, a native born American, a fireman, had suffered from the eruption for three years. He was presented as having an example of Duhring's disease of considerable severity and of wide distribution. During the past three years he had never been entirely free from the eruption but had shown partial remissions. The lesions were present on the scalp, trunk and extremities. There were numerous discrete areas of pigmentation on which "blisters" had formerly been present. The active lesions presented consisted of severely excoriated papules. The patient's general condition was fairly good.

Papulonecrotic Tuberculids. Presented by Dr. Levin.

H. E., a woman bookkeeper, aged 22, single, had suffered for four years from a recurrent eruption leaving scars on the fingers and forearms. Scattered over the forearms and dorsa of the fingers of both hands were numerous depressed scars and lentil-sized necrotic papules with firmly adherent crusts. The general examination revealed nothing abnormal, and the tuberculin test was negative.

Lymphangioma Tuberosum Multiplex. Presented by Dr. Levin.

E. B., a man, unmarried, aged 30, a clerk, an American Jew, said that the lesions appeared only eight years prior to presentation. The back of the auricle of the left ear was covered with pinhead to pea-sized globular growths;

some of these were translucent, others purplish red, and others confluent to form a hazelnut sized tumor. The front of the auricle showed two pea-sized translucent lesions, and the mastoid region was covered with one large elastic mass. The lesions were fading slowly as a result of the implantation of radium emanation. The pathology confirmed the clinical diagnosis.

PEMPHIGUS VULGARIS. Presented by DR. CANNON.

I. K., aged 54, a Jewish widow, born in Russian, with a negative family and past history; had a condition that began in December, 1924, with numerous blisters on the roof of the mouth and the mucous membrane of the cheeks and throat; this was followed by large bullous lesions on the hands, chest and back, which rapidly became generalized. She had become very weak and tired, and was unable to masticate food on account of the sores in the mouth.

Over the mucous membrane of the mouth and throat were many ruptured vesicles and bullae. Over the body and extremities were bullae varying in size from that of a small pea to that of a palm. There was no erythema around the early bullae. Nikolsky's sign was present. There were bullous lesions around the vulva and anus. The Wassermann test and urine examination were negative. Blood count revealed: white blood cells, 10,600; polymorphonuclears, 62 per cent.; small lymphocytes, 23 per cent.; large lymphocytes, 15 per cent.; red blood cells, 4,240,000; hemoglobin, 95 per cent.; blood urea and sugar, normal.

The patient had been given ferrous cacodylate intravenously, coagulen intramuscularly and alkalis, and the condition had improved greatly under treatment. Serum from blebs injected intracutaneously produced no reaction. Blood serum injected in the same way caused blebs to appear around the areas of injection.

GENERALIZED GRANULOMA ANNULARE. Presented by DR. ABRAMOWITZ.

Alice B., aged 9, born in this country, was one of six children living and well. The father and mother were Russian Jews, living and well. The mother had had two miscarriages and had lost one child by poliomyelitis and another by heart disease. The patient had had measles, varicella and pneumonia. Last winter she had pertussis, and continued to cough until three weeks before presentation, when the eruption was first noticed. The first lesion appeared on the right wrist, then others appeared on the buttocks, and now lesions were present between the thumb and index finger of the left hand, the left ulnar region and on the knees. They were circular in outline, showing at the edge a row of shiny white papules, which were slightly scaly. The centers of the lesions were clear, and they varied in size from that of a pea to 3 cm. in diameter. The patient had had pediculosis capitis and urticarial lesions on the knee and wrist for the past two weeks.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. CHARGIN.

P. R., a man, aged 33, an Austrian, a hairdresser, who was married but had no children, had a skin condition that began about eighteen years ago on both feet, and since then had spread to the upper part of both legs as far as the hip joints. The skin exhibited the characteristics of an advanced stage of the disease, showing atrophy, thinning, dryness, scaling and wrinkling, with linear areas of sclerodermatous tissue. There was some itching and burning of the affected skin. The rest of the body was entirely free. His general health was good.

A Case for Diagnosis: Acrodermatitis Chronica Atrophicans? Presented by Dr. Chargin.

T. S., a man, aged 28, a cook, had first appeared at the clinic about six months previously, presenting a typical initial lesion on the penis in which spirochetes were numerous and easily found. In the course of the general examination it was discovered that he had a condition on the hands which clinically resembled acrodermatitis chronica atrophicans. The affection involved both sides of the hand to just beyond the wrists. The skin was thin and atrophic; it could be raised from the underlying tissues and was somewhat wrinkled. The skin was purplish red, and the surface veins showed through. There was no scaling and no scleroderma. No other areas of similar character could be observed on the body. On the legs, the veins were markedly varicose, and there were numerous ulcers which were regarded as due to the vein condition. The skin on the legs was otherwise normal. The Wassermann test was 4 plus on admission. He had received twenty-one injections of bismuth and seven of arsphenamin, and at the time of presentation the Wassermann test was negative. The chancre healed promptly under the treatment.

DISCUSSION

Dr. Rostenberg: I do not doubt the diagnosis, but I believe the ulcerations are syphilitic, implanted on the other lesions.

Dr. Maloney: The lesions on the hands look like a beginning acrodermatitis, but those on the legs look like syphilis.

Dr. Chargin: The condition on the hands is especially interesting, in that clinically it resembles the skin observed in acrodermatitis chronica atrophicans. This disease is occasionally limited to the hands. The patient is a Turk and it is impossible to get a good history, but on clinical grounds alone it seems justifiable to make the diagnosis of acrodermatitis chronica atrophicans on account of the characteristic appearance and the history of long duration. It is possible that the affection began following a traumatic wound to the hands. I am of the opinion, however, that the ulcers and scars on the lower extremity are not syphilitic but due to the varicose veins. The syphilis is not of more than six months' duration, and the ulcers and sores were observed at the time of the presence of the chancre.

Xanthoma Tuberosum Multiplex. Presented by Dr. Chargin.

F. Z., aged 27, married, an engineer, had a disease that began six months prior to presentation, and which was first noticed on the palms. The lesions were a lemon-yellow, millet seed to pea size, numerous and soft to the touch. They were especially numerous and were distributed in linear form in the flexures of the fingers, where they caused considerable inconvenience when the patient was handling things. Otherwise the patient was in good health. The mucous membranes were free. The urine showed no sugar or albumin. The blood sugar was 110 mg. per one hundred cubic centimeters of blood; the blood cholesterol was 3.5 per thousand.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, May 11, 1925

EDWARD F. CORSON, M.D., *Presiding*

A CASE PRESENTED FOR DIAGNOSIS. DR. GREENBAUM.

J. S., a girl, aged 15, complained of intense itching. The trouble began at the age of 2 years. At the age of 11, it went away entirely for two years, then recurred. This recurrence was about the time she began to menstruate. She had had three or four other remissions of approximately a month's duration. There was no exaggeration of symptoms at the menstrual period, but the symptoms were more pronounced during extremes of temperature and after eating strawberries or peaches. The itching was worse at night. The lesions consisted of excoriated papules scattered over the body, but worse on the neck, back, arms and legs. There was no history of vesiculation. There was a lichenified plaque over the nape of the neck. The past history was uneventful. Tonsillectomy had been performed when she was 5 years old. She had had a goiter the preceding year, which had been treated by the roentgen ray. The family history was negative for dermatoses. A complete blood count showed nothing abnormal, except in one instance, when 9 per cent. eosinophils appeared. Another count showed 3 per cent.

DISCUSSION

DR. STOKES: I was inclined at first to make the diagnosis of dermatitis herpetiformis, but I changed my view because of the type of the lesion and the distribution. I thought the condition might be classified as lichen urticatus.

DR. WEIDMAN: I agree to the diagnosis of lichen urticatus.

DR. SCHAMBERG: The case is difficult to classify. The patient had an itching, long standing, papular eruption; her skin was abnormally dry. She had enlargement of one lobe of the thyroid, and he thought that possibly the condition depended on the thyroid disturbance. In thyroid disturbances the skin and hair were always dry. The fissures in the skin might suggest hypothyroidism.

DR. CORSON: I at first thought the condition was dermatitis herpetiformis, but I believed that neurodermatitis should be considered.

A CASE PRESENTED FOR DIAGNOSIS. DR. SCHAFFER.

C. W., a colored woman, was presented because of translucent papular lesions on the face, associated with depigmentation. The condition began in November with a group of close-set papules, with depigmentation on the upper lip. There was another patch of typical leukoderma in the malar region, to which the pigment had since returned. There were practically no symptoms. The Wassermann test was negative. A biopsy had been taken.

DISCUSSION

DR. WEIDMAN: There is no change in the epidermis. The nodule consists of an infiltration of lymphocytes; there is interstitial edema, few epithelioid cells and rarely a giant cell. Most unusual is the presence of cavernous spaces, which evidently contain lymph—at first glance they look like fat cells, but on closer observation they are seen to connect with lymph channels, and in places are lined with endothelium. This picture does not help in the diagnosis—if syphilis or tuberculosis, it is histologically too early a picture to be characteristic.

DR. CORSON: Should syringocystoma be considered from the appearance of the section?

DR. WEIDMAN: The picture does not resemble that of syringocystoma.

DR. SCHAMBERG: The rapidity of development and the appearance of isolated, scattered lesions, speak against tuberculosis, and the clinical picture is certainly not that of syphilis. Would not lymphangioma circumscriptum multiplex be consistent with the pathologic findings?

DR. WEIDMAN: The picture would not be consistent with that diagnosis. The inflammatory element is out of all proportion to the vascular element, and some sections show no dilated lymph spaces. If lymphangioma circumscriptum multiplex is to be considered, this case will help to explain its cause—pressure on the lymphatics by cellular infiltration, that is, an inflammatory and not a neoplastic basis.

DR. SCHAFFER: The patient developed lesions which involuted, leaving patches of leukoderma in which the pigmentation returned. Ammoniated mercury was applied locally, and on the chin one-half erythema dose of radium, screened, was applied. The Wassermann test was carefully checked. At the time of the first appearance in January, the body showed no lesions.

DR. GREENBAUM: In view of the lack of effect by mercury and radium, I would suggest that when the lesions are destroyed, curettage be the method used, and that guinea-pig inoculation be carried out with the material obtained.

DR. STOKES: The possibility of lichen nitidus is suggested histologically, though this is not the clinical situation for a typical example of this condition.

DR. CORSON: Temporary leukoderma is of common appearance in the colored race. I recently saw a second patient with vitiligo which completely obliterated a lupus erythematosus.

NEUROFIBROMATOSIS. Presented by DR. GREENBAUM for DR. KLAUDER.

J. F., a colored man, aged 33, had had the condition since the age of 10. The pigmented lesions preceded the development of the neurofibroma. Recently two patients with pigmentary changes plus mental changes of neurofibromatosis had been seen in his own practice, who showed no tumors.

DISCUSSION

DR. WEIDMAN: In these cases, careful inquiry should be made for the presence or absence of visceral symptoms. In two cases under my observation which came to necropsy visceral lesions were found in the stomach, intestines and bladder. The matter of mental symptoms was made more understandable from the occurrence of a case of widespread meningeal nevic pigmentation reported by Dr. Eiman. The child died with nervous symptoms. She also had extensive nevi in the skin.

DR. GREENBAUM: I wish to call attention to the congenital defect of the superior and inferior maxilla showed by the patient under discussion.

DR. DENGLER: A patient with nerofibromatosis, under my care, has total alopecia.

DR. SCHAMBERG: In Recklinghausen's disease there is a profound basic disturbance, perhaps of the endocrine glands. Dr. B. C. Hirst reported cases of fibroma acuminata occurring during pregnancy, lasting some months and then disappearing. The occurrence of fibromas at a time when there is a distinct drain on the endocrine system, and their disappearance on the cessation of that

drain, suggests that possibility. Lipomas have been seen in various parts of the body, as well as fibromas, and often there have been coincident evidences of mental deficiency.

MOLLUSCUM CONTAGIOSUM. DR. WEIDMAN.

Dr. Weidman showed a chicken which had been inoculated with the chicken strain of *Molluscum contagiosum*, and remarked on the superficial resemblance between it and the human form of chickenpox. He did not believe that the two diseases were identical.

PATRICIA HART-DRANT, Secretary.

MANHATTAN DERMATOLOGICAL SOCIETY

Regular Meeting, May 12, 1925

MAX SCHEER, M.D., *President*

CHLOASMA. Presented by DR. GILMOUR.

A woman, aged 35, came to the clinic on Feb. 8, 1922, presenting a condition of the scalp which was diagnosed as seborrhea, also a darkening of the skin on the chin and forehead which was covered with very fine gray scales. The Wassermann reaction was negative. The urinalysis also was negative. Under treatment the seborrhea improved, but the pigmentation was no better. These darkened areas were interesting in that they were covered with scales limited to the pigmented areas. Various applications were made and the scales disappeared, but the pigmentation has remained unchanged since its first appearance three years ago.

DISCUSSION

DR. MCGLASSON (San Antonio, Texas): The case is interesting. The condition appears to be merely a chloasma, but apparently there is some hypertrophy, which may be due to the treatment.

DR. WISE: The discoloration is probably due to the use of cosmetics.

DR. BECHET: I agree with Dr. Wise. Several cases have been shown within the past few years in which there have been similar reactions to the varied applications of the innumerable "beauty" lotions and salves used by women. There seems to be less pigmentation than in ordinary chloasma.

DR. ANDREWS: I agree with Dr. Wise and Dr. Bechet. Many cases are noted in the literature. This woman had hypertrichosis, which may account for the use of some cosmetic.

DR. OCHS: I believe the condition is due to some cosmetic.

DR. LEVIN: The skin shows areas of pigmentation which might develop after the application of a cosmetic or after any other form of repeated irritation from the application of a chemical.

DR. SATENSTEIN: We used to see a number of such cases in the old days when beta naphthol was used for peeling the face. This particular patient has used an ointment containing beta naphthol since last November (office record).

DR. GILMOUR: When the patient first came for treatment she admitted using hair dye; the condition might be due to that. At first it was supposed to be a seborrhea plain and simple, but the condition never cleared up.

SARCOID: DARIER-ROUSSY TYPE. Presented by DR. LEVIN.

The patient was previously shown at the Dermatological Section of the New York Academy of Medicine and the New York Dermatological Society. He was presented again to show the good effect resulting from intramuscular injections of a 2 per cent. solution of sodium arsenite. The lesions were half of their size as first observed, the infiltration had greatly diminished, making the lesions appear superficial.

DISCUSSION

DR. SATENSTIEN: Why does Dr. Levine consider it to be of the Darier-Roussy type? We have seen four cases during the last four years which showed deep infiltration, sometimes solid plaques suggesting leukemia. This case should be classified as of the superficial type. As for therapy, sodium arsenite sometimes is very effective; it should be tried.

DR. LEVIN: I presented the case as a Darier-Roussy type of sarcoid, because when the patient first appeared the lesions were not superficial but penetrated almost to the muscles, and if a lesion were grasped between the fingers it felt like a paraffinoma. The course of the lesions and the tendency to disappearance resembled a case of Darier-Roussy which I presented two years before. As the lesions tended to disappear, they seemed to become more superficial and assumed the appearance of sarcoid of Boeck. The pathology confirmed the diagnosis.

HYPERTROPHIC LICHEN PLANUS. Presented by DR. ROSEN.

A man, aged 52, presented an eruption on the inner surface of the left leg, clinically characteristic of lichen planus verrucosa. The condition was of nine months' duration, and the case was presented with a request for suggestions as to treatment.

DISCUSSION

DR. OCHS: I like to use pure phenol on such lesions. In several such cases I did not even neutralize the phenol, and the lesions disappeared.

DR. BECHET: A case shown at the New York Dermatological Society responded favorably to treatment with mercuric salicylarsenate.

DR. LEVIN: I have noted good effects with arsenic therapy.

DR. WISE: If I had another case I would try Dr. Ochs' suggestion about phenol, though I suspect that it would not cure a lesion like this one; I would first give a full unit of filtered roentgen ray once a month for two treatments and give arsenic injections.

DR. ANDREWS: This lichen planus lesion is unusually hard, and quite red and vascular. I believe that this type, so actively inflammatory, responds better to the roentgen ray than those in which there is not so much redness. I should like to know what the members think about giving potassium hydrate before using the roentgen rays.

DR. SATENSTEIN: I agreed with what Dr. Andrews has said. It does not so much matter what is used; it is a question of getting rid of the thickened epidermis. I have used dilute trichloracetic acid, pure phenol, etc., and the

results have been about the same; I then used filtered roentgen rays, and the lesions almost disappeared; but they are not cured.

DR. WALLHAUSER: I have tried various methods of cauterization without benefit; in my experience, roentgen-ray treatment has been most successful.

DR. ELLER: I should not be surprised if electrocoagulation would prove a good mode of therapy in this particular case, either monopolar or bipolar, for by this surgical method one treatment would suffice. It would save a great deal of time. If roentgen-ray therapy were used, it would take several months or more for the lesion to disappear.

DR. SATENSTEIN: Has any one seen a real cure in these cases?

DR. ROSEN: I am glad to have heard some of the remarks and suggestions in regard to therapy for the type of lesion presented by the patient. I did not think the case would bring out so much diversity of opinion as to therapeutics. I had no difficulty in treating other patients who had hypertrophic lichen planus with unfiltered roentgen rays. Of course in the present case the lesion is marked, but I am inclined to carry out the suggestion of Dr. Wise and Dr. Andrews and use unfiltrated rays for several weeks. I do not care to use electric coagulation on this patient, for there is very poor circulation in the tissue, and since with electric coagulation the healing is very slow, it might be months before it healed.

DR. MCGLASSON: I have seen similar lesions disappear under treatment with unfiltered roentgen rays.

GUMMAS. Presented by DR. LEVIN.

A. M., a woman, aged 21, married, a native of Germany, came to the clinic the day prior to presentation, and gave a history of having had ulcers of the legs for one week. Similar lesions had been present a year before and had healed spontaneously. Both legs, but mainly the left, presented several nickel to quarter dollar sized, clean, punched-out ulcers, with a sero-purulent discharge. There were also numerous lentil to pea-sized deeply punched-out ulcers. Scattered over both legs were numerous round and reniform pigmented scars. The lesions were most evident on the lower dorsal aspects. The left forearm was covered with several dozen lentil-sized pigmented scars grouped in annular arrangements and segments of circles. Similar scars were found grouped on the back of the index finger. The Wassermann test was 2 plus.

DISCUSSION

DR. MCGLASSON: The lesions on the arm appear to be papulonecrotic tuberculids, while those on the legs appear to be typical syphilids—two conditions.

DR. WISE: I believe that the lesions on the arm are papulonecrotic tuberculids, but I believe the differentiation of the lesions on the leg is impossible clinically. I am inclined to believe that they are all tuberculous.

DR. WEISS: I agree with Dr. Wise. I believe that all the lesions are papulonecrotic tuberculids.

DR. WALLHAUSER: The serpiginous lesion on the forearm resembles a syphilitic lesions, but the question cannot be decided until a therapeutic test has been made.

DR. PAROUNAGIAN: Like Dr. McGlasson, I believe that two conditions are present, syphilis and tuberculosis. I do not consider the ulcers of the leg entirely syphilitic in origin, for the ulceration is more on the calf of the leg.

The patient no doubt has syphilitic lesions, especially on the forearm—a papulonecrotic tuberculid on the upper portion of the arm near the elbow. The only way to decide the question is to do as suggested and give antisyphilitic treatment; the lesions that do not clear up are tuberculous.

DR. OCHS: I agree with Dr. Wise that all the lesions are papulonecrotic tuberculids.

DR. ELLER: It is almost impossible to make a diagnosis of the lesions on the legs without a therapeutic test. I do not think that a Wassermann test or a biopsy would help very much. The lesions on the upper extremities are papulonecrotic tuberculids.

DR. GILMOUR: The case is a most interesting case. I believe the lesions on the arms are tuberculids, but I am not sure about those on the legs. One opinion is as good as another.

DR. KINGSBURY: I consider the whole condition syphilis; the duration of the lesions on the arms is too short for tuberculid. Probably the whole condition dates from marriage. In my opinion, antisyphilitic treatment is indicated.

DR. MOUNT: I agree with Dr. Kingsbury that the entire condition is syphilitic. I can see no evidence of papulonecrotic tuberculid.

DR. BECHET: It is a well-known fact that papulonecrotic tuberculid is sometimes protean in its manifestations. The lesions on the backs of the hands are indolent and show some necrotic changes. There are typical vacciniform scars around the elbows and purplish lesions on the calf of the leg, with a punched-out appearance. The fact that the eruptions occurred simultaneously is also in favor of tuberculosis. It is a most interesting case, and I favor the diagnosis of tuberculid rather than syphilis.

DR. ANDREWS: The case requires further study before a definite diagnosis can be made. The Wassermann test is not conclusive, for a two plus Wassermann reaction is common in tuberculids, and tuberculids may also disappear under antisyphilitic treatment. If the papular lesions on the hands are tuberculids, they may very well disappear under treatment with arsenic. One would have to continue the Wassermann test, make a therapeutic test and perform a biopsy before reaching a definite diagnosis.

DR. MCGLASSON: No one has spoken about the scars of the healed lesions on the legs, which are characteristic of healed syphilitic lesions.

DR. MOUNT: The therapeutic test should be made with mercury alone or with mercury and potassium iodid, not with arsenic.

DR. PAROUNAGIAN: I think that arsphenamin should be given.

DR. SATENSTEIN: I wonder how the impression has been gained that the microscope will not help. Several of the speakers have made that statement. The pathology of the superficial gumma is fairly characteristic, and the pathology of Bazin's disease is fairly definite. The difference between the two is so great that it is astonishing to hear that the microscope will not help. I have not heard any one suggest the possibility of still another diagnosis, that of simple periphlebitis associated with the early breaking down of a deep inflammatory process. The lesions on the upper extremities may be simple papulonecrotic tuberculids; it may be that the whole condition is nonsyphilitic and nontuberculous.

DR. LEVIN: The patient was admitted to the clinic one day prior to presentation. She said that she had had similar lesions a year before, which had

healed, and that the ulcers now presented appeared a week before presentation. My tentative diagnoses to the students are two: possible tuberculosis, an erythema indurata, or syphilis; I have also thought of the possibility of periphlebitis. The points in favor of erythema indurata are the patient's age and sex and the distribution of the lesions. On examination she presented clean-cut punched-out ulcers, not on the calves but on the lower part of the legs. On further examination, several lentil-sized, deeply punched-out ulcerations without any undermining of the edges and irregularity as are found in erythema induratum, were observed. On the upper extremities were small scars with pigmentation, the results of what were probably punched-out gummatous lesions. Arsenic will clear up tuberculous as well as syphilitic lesions, and I suggested the use of bismuth in the treatment. Her Wassermann test proved to be two plus, and is considered positive for syphilis at Cornell, where an alcoholic antigen is employed. Periphlebitis shows acute inflammation along the course of the veins and does not show the clean-cut lesions presented by the patient.

We shall put the patient on bismuth therapy and make a complete examination, and I shall report the biopsy findings. Meanwhile, I consider the condition syphilis.

REINFECTION. Presented by DR. LEVIN.

E. A., an American, aged 36, was infected and had an intra-urethral chancre in September, 1923. The eye, nerve and general medical examinations were all negative. He received six intravenous injections of arsphenamin and numerous mercury rubbings. He had also worn mercury in contact with the skin. In November, 1923, the Wassermann reaction was negative, and again on three other occasions — the last on May 5, 1924. Lumbar puncture in 1924, showed a normal spinal fluid. He was exposed to infection three months before presentation, and three weeks later developed a lesion on the prepuce. Three weeks later he had a generalized eruption. The Wassermann test, at first negative, was now positive. As presented, the skin disclosed a generalized symmetrical, scaly, papular, syphiloderm, involving also the palms, a generalized adenopathy, and a healing lesion of the penis. He had recently received two injections of arsphenamin and two of mercury.

DISCUSSION

DR. ROSEN: The case is very interesting. I agree with the diagnosis as presented.

DR. LEVIN: When I first saw the patient on readmission he was under treatment in the genito-urinary department for gonorrheal urethritis, and showed a large indurated ulcer involving the prepuce and the glans. At first I considered it as possibly being a tertiary lesion, but under observation the patient developed the lesions of the secondary stage of syphilis, including the intensive scaly, papular eruption, and a positive Wassermann test.

PARAPSORIASIS. Presented by DR. ELLER.

The case had previously been presented at the last meeting, with a tentative diagnosis of parapsoriasis, which proved to be correct according to the pathologic report. Mycosis fungoides and Hansen's disease were also considered.

DISCUSSION

DRS. WISE, ROSEN and MCGLASSON agreed with the diagnosis.

DR. SATENSTEIN: I have been much interested in the problem of premycosis and have been studying a good deal of tissue. The majority of the reports in the literature at this stage state that there is no pathology on which one can make a diagnosis. The pathology is a simple inflammation with the usual changes of a long standing inflammation, in the epidermis, i. e., in the upper cutis there is the ordinary pathology of chronic eczema. A diagnosis of mycosis cannot be made, because it does not exist under the microscope. Making a clinical diagnosis at this stage is equivalent to the clinical verdict of "guilty, but not proved." There is no way of proving it at this stage. It is simply a clinical guess. In this particular case a simple inflammatory process is present as just mentioned; it is a familiar type, as seen in parapsoriasis, so for the want of something better it is reported as parapsoriasis; a few years hence, it may not be parapsoriasis. There is no suggestion of leprosy. The diagnosis is only a clinical one.

DR. LEVIN: How does Dr. Satenstein differentiate between parapsoriasis and seborrheic eczema under the microscope, without special staining. Both conditions belong to the parakeratotic group, and it is essential to show absence or presence of follicular or hair changes.

DR. SATENSTEIN: The diagnosis is usually based on the paucity of the findings rather than on any positive evidence.

DR. ELLER: I shall follow the suggestion of some of the members and give pilocarpin injections. The result of this treatment will be reported at the next meeting.

ANGIOMA SERPIGINOSUM. Presented by DR. OCHS.

The patient, a young man, was previously presented at the Section on Dermatology and Syphilis at the New York Academy of Medicine on May 5, with lesions on both sides of the face near the eyes, which had been present for about a year. He was a printer and was accustomed to working under a strong, steady light. During the day one could readily see the red-pepper spots, also some skin which had not yet become affected, and new blood vessels. At the New York Academy of Medicine the case had been presented with a diagnosis of angioma serpiginosum, and it was again presented with the same diagnosis.

DISCUSSION

DR. WEISS: I am ready to concede that this may be an actinic lesion in view of the patient's exposure to light. Since telangiectasis results from roentgen-ray treatment, it is possible that these lesions might have resulted from a similar cause although of different origin. I would not call a roentgen-ray telangiectasis angioma serpiginosum, but I would designate it as telangiectasis ab luce, through the cathode rays. The lesions in this case are confined to the most exposed portions of the patient's face, where the actinic days of the electric light exert their deleterious influence.

DR. WISE: I agree with Dr. Weiss that the condition is probably an actinic dermatitis. The diagnosis of angioma serpiginosum is made with ease on account of the vascular dilatation present in the form of actual capillaries which can be seen at a distance — not a diffused dermatitis such as this man presents.

DR. MCGLASSON: I agree with most of the speakers; I cannot believe that this is a case of angioma serpiginosum. In my section of the country where most of the people lead an active outdoor life, such conditions are seen all over the face.

DR. BECHET: I agree with Dr. McGlasson and Dr. Wise that the condition is an actinic dermatitis. I presented a patient some years ago who had similar lesions, with the tentative diagnosis of angioma serpiginosum. Dr. Ochs' patient was a linotype operator, and gave a history of prolonged exposure to the electric light. The lesions appear to be identical with those so frequently observed on the sternoclavicular junction of women after an all summer exposure.

DR. BECHET: My patient also was exposed to strong electric light, and I believe the two conditions are identical and due to the same causative factor of strong electric light.

DR. GILMOUR: I believe that it is an actinic dermatitis; the history supports that view. For the last three or four years the man has used colored glasses, and the parts covered by the glasses are free from the lesions, while those exposed are erythematous. The line of demarcation between the area protected by the glasses and the exposed portions is a sharp one.

DR. LEVIN: I saw the patient previously and suggested the possibility of lupus erythematosus of the telangiectatic type or an actinic dermatitis. I again suggest lupus erythematosus of the telangiectatic type. Near the left corner of the mouth there is a dark red, scaly lesion, and on the left palm there is a lesion occasionally observed with telangiectatic lupus erythematosus. I believe the patient should be watched for the development of further lesions of lupus erythematosus.

DR. MCGLASSON: A patient recently presented at a meeting of the Texas Dermatological Association who had been in an institution, for the tuberculous had regained normal weight, and had been discharged as having an arrested case. She had been treated by an air cooled mercury vapor lamp by another physician for an undetermined condition. Just where the lead shield eye piece was fitted was a perfect curve presenting a scaly lesion which appeared to be lupus erythematosus. She said she had been given about fifteen treatments, and did not have the scaling before; and that it appeared exactly around the curve of the eye piece. Referring to the lesions on the palms, Dr. McGlasson said that every linotype operator presents horny lesions on the palms from striking the bar of the linotype. The statement of the patient should be taken with a grain of salt. I do not doubt the possibility that the condition developed from injuries caused by light.

DR. OCHS: I am glad that I brought up the case. As for its being an actinic dermatitis, the young man does not wear a shield. Why should we have the condition only on both angles of the eyes? He has been working for only a year, and says that he has noticed the pin-point eruption at both sides, and that it is extending. Examination in daylight showed small red-pepper points and areas not covered with telangiectasia. I regard the condition as angioma serpiginosum, but I shall watch the patient in view of the suggestion made by Dr. Levin, and I shall try to present him again in the fall.

PURPURA ANNULARIS TELANGIECTODES. Presented by DR. BECHET.

B. S., a man, aged 28, came to Dr. Whitehouse's service stating that he had an eruption which had been present for three months. He denied having

taken any internal medication either before or after the appearance of the lesions. On the legs and trunk were a large number of reddish-brown patches with a ringlike aspect. Their centers were a fading yellow, with pinhead sized telangiectoid spots on the peripheral portion. In some patches the annular formation was lacking and an elongated form assumed. A few patches showed some scaling. Some of the older lesions were light brown.

DISCUSSION

DR. WEISS: The case presents all the attributes of real Majocchi's disease, showing the fine cayenne pepper points, grouped and annular lesions, beginning alopecia and atrophy, etc. Clinically, it is a clear case of Majocchi's disease, and it is very gratifying to have been able to see it again, as I have not seen a case for the last three years. Those that have been presented have all been more or less doubtful.

DR. PAROUNAGIAN: I disagree with the diagnosis of Majocchi's disease. If this were a case of Majocchi's disease, then the case which I presented as Majocchi's disease, and which was generally accepted as such, was not a case of that disease. Dr. Andrews is familiar with the case. I failed to see any resemblance between Dr. Bechet's case and the one which I presented.

DR. LEVIN: I disagree with the diagnosis of Majocchi's disease. I do not know what to call it, but it is not Majocchi's disease.

DR. BECHET: I have seen a number of cases presented as Majocchi's disease that did not coincide with the descriptions of Weiss and MacKee in their respective articles, but the case under consideration certainly does. In daylight the "red-pepper-like points" show distinctly and are annular in distribution. Some of the patches are reddish brown, others pigmented, and still others slightly scaly. The objective symptoms therefore are characteristic of the disease and warrant the diagnosis offered.

DOUBLE CHANCRE OF LIP. Presented by DR. PAROUNAGIAN.

F. R., a girl, aged 18, who presented herself at the clinic, had two lesions, one on the upper and the other on the lower lip, the duration of which was said to be about two weeks. The glands at the angle of the jaw (left side) were markedly swollen. The patient said that the first lesion appeared on the upper lip and the second one a week later on the under lip. Darkfield examination was positive from both lesions, and there was no evidence of eruption on the body.

The source of infection could be traced, as the person who referred her to the clinic was another patient who made his first visit on April 3, 1925, also with a chancre on the lip and secondary manifestations.

SCLERODERMA AND FACIAL HEMIATROPHY. Presented by DR. ANDREWS.

The patient, a woman from the Vanderbilt Clinic (previously presented by Dr. Parounagian and Dr. Levin), had an eruption on the left of the frontal region of the scalp, of seven years' duration, without any predisposing cause. A diagnosis of scleroderma was made. The eruption on the face had appeared at intervals for the past five years, and a diagnosis of rosacea was made. There was no history of any change in the general health coincident with the onset of either eruption. There was a depression of the frontal bone associated with the strip of scleroderma of the scalp, and paralysis of the sympathetic nerve of the left eye.

DISCUSSION

DR. LEVIN: I presented this patient before the skin section of the Academy about four years ago. She then showed hemiatrophy of the left side of the scalp and face, with patches of morphea on the back and right arm. Improvement had followed thyroid therapy. A roentgenogram of the skull showed nothing abnormal.

DR. PAROUNAGIAN: I saw the patient ten years ago at Gouverneur Hospital, and I presented the case at the New York Academy of Medicine.

DETROIT DERMATOLOGICAL SOCIETY

Regular Meeting, May 19, 1925

UDO J. WILE, M.D., *Presiding*

ICHTHYOSIS HYSTRIX. Presented by DR. WILE.

M. S., a schoolgirl, aged 12, said that the skin condition had been present since birth; it was asymptomatic and not progressive. There was a generalized, dry, noninflammatory scaling of the skin, the scales being closely adherent over the extremities. The entire trunk, and especially the neck and axillae, presented some hyperpigmentation, which was definitely linear over the abdomen. There were minute, pinhead-sized, papillary excrescences about the neck, axillae and abdomen, and the histologic picture was that of a papillomatous hyperplasia with hyperkeratosis. No active chromatophores were found.

ACANTHOSIS NIGRICANS, JUVENILE TYPE. Presented by DR. WILE.

L. S., a schoolgirl, aged 14, in 1920 first noticed an increase in pigmentation about the neck, axillae and other normally pigmented areas. This condition had progressed and become generalized, varying from brown to black, and being especially pronounced in the flexures, about the nipples and the external genitalia. In these locations, and about the neck, the natural lines of the skin were exaggerated, and there were innumerable tiny papillary growths. The mucosae showed little increase in deposit of pigment. There was a definite loss of axillary and genital hair, and the hair of the scalp was considerably thinned.

DISCUSSION

DR. PARKHURST: There is a striking similarity between these two cases, although the first is apparently one of ichthyosis; the second case is a very good example of acanthosis nigricans of the juvenile type.

DR. WILE: The second case is a classical example of acanthosis nigricans, which in children usually is not associated with malignancy. The first case presented a different picture before treatment was started: a typical ichthyosis hystrix.

PEMPHIGUS VULGARIS OR DERMATITIS HERPETIFORMIS? Presented by DR. WILE.

M. M., a schoolgirl, aged 14, who first appeared at the University Hospital Clinic in 1923, one year prior to that time had a generalized pruritus, followed by a more or less generalized miliary eruption. Small and large vesicles

soon appeared, three outbreaks having occurred during the first year. The eruption apparently did not undergo complete involution, a few bullae and crusts persisting from one attack to the next. During her stay in the hospital, there was a continuous cycle of outbreaks and remissions, varying in duration and intensity, and all associated with some pruritus and resultant pigmentation. The bullae were of various sizes, the largest attaining the size of a silver dollar; they were frequently linear and sausage shaped. The mucosae were not commonly involved in the attacks. At the time of presentation, there were a few bullae, apparently arising from normal skin, their contents rapidly becoming purulent. Over the extremities were numerous irregularly shaped and linear crusts from previous lesions. The weight and continued development of the patient was normal.

DISCUSSION

DR. SCHILLER: This is probably a case of dermatitis herpetiformis.

DR. WOLLENBERG: The present absence of itching suggests a diagnosis of pemphigus.

DR. WILE: The diagnosis is not clear in this case. The condition is either very slow pemphigus or dermatitis herpetiformis. There are remissions, and it is absolutely resistant to all forms of treatment. Arsenic is of no avail. I would favor a diagnosis of pemphigus rather than dermatitis herpetiformis.

DR. BARTHOLOMEW: Has mercurochrome-220 soluble been used in this case?

DR. WILE: Yes, but with no result.

LEPRA OF THE MACULO-ANESTHETIC TYPE. Presented by DR. WILE.

J. K., a Syrian laborer, aged 30, had come to the hospital because of weakness and swelling of the hands and feet. He had immigrated to America seventeen years previously, and his first symptoms had occurred at the age of 20, when he noted numbness of the last two fingers of each hand. For eight months he had been unable to work, because of swollen extremities and asthenia. He was poorly nourished. On the trunk there were many silver dollar to palm sized, nonscaling, erythematous patches, each of which was slightly anesthetic to pain. The hands and feet, and to a lesser extent the face, presented a diffuse swelling, which did not pit on pressure, and was evidently due to hyperplasia of the connective tissue. The hands and feet apparently had lost the sensation of pain. Histologic examination revealed the characteristic lesions of early lepra, and a large number of lepra bacilli were found.

MULTIPLE BENIGN CYSTIC EPITHELIOMA. Presented by DR. WILE.

W. S., a farmer, presented a large tumor mass in the upper left quadrant of the abdomen; apparently it was neoplastic. Over the upper part of the abdomen and lower part of the chest were half a dozen subcutaneous nodules, varying in size from that of a glass pinhead to that of a pea. They were reddish brown, noninflammatory, painless and apparently not attached to the overlying skin. The duration of these nodules was unknown, but the patient believed that they had recently appeared. Histologic examination revealed the diagnosis.

DISCUSSION

DR. JAMIESON: I should have hesitated to make a diagnosis in this case without the aid of a biopsy examination.

LYMPHOBLASTOMA: LEUKEMIA CUTIS OF ALEUKEMIC TYPE. Presented by DR. WILE.

J. M., a laborer, aged 64, had noticed generalized pruritus about seven months previously; there had been some itching of the extremities for three years. He had lost some weight and had become quite weak. During the period of seven months a copper-brown pigmentation had appeared, especially on the trunk, associated with much scaling and infiltration, together with numerous fine telangiectases. An extensive papillomatous overgrowth covered the wrists and the dorsal surfaces of the hands, feet and ankles. The superficial lymph nodes were enlarged, the inguinal nodes having reached the size of a small lemon. There were 3,424,000 red blood corpuscles, 2,400 white blood cells, and a differential count showed polymorphonuclear leukocytes, 51 per cent.; basophils, 1 per cent.; eosinophils, 12 per cent.; large lymphocytes, 12 per cent.; small lymphocytes, 17 per cent. and large mononuclear cells, 8 per cent. The red blood corpuscles showed slight achromia.

MULTIPLE THROMBOTIC ULCERATION, SIMULATING NODULO-ULCERATIVE SYPHILODERMA. Presented by DR. WILE.

J. S., a decorator, aged 59, said that during the previous fifteen years he had had three outbreaks of ulcers of the leg. The lesions presented were of six weeks' duration. Involving the lower one-third of the right leg in its external aspect, was an ulcer twice the size of a palm, with a serpiginous, slightly punched-out border. Outlying this lesion were three similar quarter dollar size, punched-out ulcers. Clinically, the picture was that of nodular ulcerative syphiloderma. Pathologically, however, these lesions showed chronic ulcers with vascular pyogenic granulation tissue. No tubercles nor any evidence of specific granuloma were found. The blood Wassermann reaction and the spinal fluid examination were negative. Radiographically, there was no bone involvement, and antisyphilitic treatment had not influenced the course of the ulceration.

ADDISON'S SYNDROME. Presented by DR. WILE.

P. S., a farmer, aged 40, had first noticed the appearance of hyperpigmentation at the age of 20. During the ten years prior to admission, it had progressed, becoming generalized, and the patient had become too weak to work. The coloration was bronze, being most marked on the face and hands and at the sites of normal pigment deposit. Other than the increase in pigment, there was no change in the skin. The mucosae of the cheeks and lips were also hyperpigmented. The blood pressure was 88 systolic and 72 diastolic.

LUPUS ERYTHEMATOSUS. Presented by DR. WILE.

E. D., a plumber, aged 36, said that the eruption had been present for seven years. On the dorsa of the fingers, and especially on the proximal phalanges, were many hyperkeratotic follicular plugs. The dorsa of the hands and the extensor surface of the arms presented a diffuse slight erythema, with atrophy and an adherent silvery-white scale. On each cheek, just anterior to the ear, was an atrophic scar the size of a dollar. There were also a few lesions on the right shoulder. Following the removal of one devitalized tooth, there was a definite tendency toward involution of the eruption.

LUPUS ERYTHEMATOSUS OR PITYRIASIS RUBRA PILARIS? Presented by DR. WILE.

A. K., a schoolboy, aged 17, had entered the hospital because of weakness and an eruption involving the face, hands, forearms and shoulders. It had

first appeared two years previously, during an attack of "rheumatic fever." The patient was undernourished and had lost weight. The eruption consisted of a dull red to pink erythema, with a very fine, thin, closely adherent scale. Over the forehead there were many hyperkeratotic plugs, and the process was definitely associated with atrophy. Over the phalangeal and metacarpal articulations, the skin was more brightly erythematous, with some infiltration, and it was definitely atrophic. Complete and detailed physical and laboratory examination had failed to reveal any cause for the loss of weight and weakness.

DISCUSSION

DR. VARNEY: The adult had a typical tuberculid, while the eruption in the boy was more difficult to interpret. The patches about the boy's neck resembled those of morphea, but the condition was apparently lupus erythematosus.

DR. WOLLENBERG: The patches on the man's face were characteristic of lupus erythematosus, and probably the lesions on the arms were papulonecrotic tuberculids, being due to the same tuberculous toxemia.

DR. PARKHURST: I found no papules on the man's hand or arms, but there were adherent scales with follicular plugs, suggesting that this was a case of disseminated lupus erythematosus. The boy seemed to have the same condition.

DR. WILE: In the boy's case there was a peculiar reticulated atrophy like that of early acrodermatitis chronica atrophicans.

LICHEN PLANUS; ARSENICAL PIGMENTATION; LEUKODERMA. Presented by DR. WILE.

A. W., a realtor, aged 51, said that he had had the original eruption at the age of 11; it had begun over the tibiae and had remained localized for twenty years. At the age of 31, he had been confined to bed with a vesicular and bullous eruption. The eruption at the time of presentation was extremely pruritic, and treatment of various kinds had brought no relief. The patient was well nourished, with an extensive hyperpigmentation, chiefly involving the extremities. Associated with this process were many areas of total depigmentation from dime to palm size. Interspersed throughout the pigmentary changes, but especially over the legs, extensor surface of the forearms and the region of the coccyx, were many irregularly round, violaceous papules from pinhead to pea size. Here there had been a great deal of scratching, and the unscratched papules showed a rather definite sheen. Involving the entire dorsum of the tongue was a silvery white, closely adherent, rather superficial parakeratosis.

SYPHILIS MUTILANS. Presented by DR. WILE.

Mrs. I. W., soon after her marriage nineteen years previously, had noticed genital lesions, which had disappeared under local treatment. Eight years before presentation, a small nodule had appeared over the right eye. This had slowly enlarged, broken down and extended until the entire face was involved. Spontaneous healing occurred, but there was always an area of activity which was extending and destroying. At the time of presentation there was a markedly destructive process involving the entire face and scalp. The outer table of the skull, extending posteriorly from the glabella to the occiput, had been entirely destroyed by the process, and many irregular dis-

charging sinuses were present. The entire nose had been destroyed, and both cheeks presented atrophic scarring with many telangiectases, the healing process extending posteriorly as far as the ears. The left eye had been destroyed, while perception still remained in the right. Here the globe was markedly protruberent, giving the patient an extreme exophthalmos. The Wassermann reaction of the blood was strongly positive.

GRANULOMA ANNULARE? Presented by DR. DOTY.

A schoolboy, aged 12, of average weight and in good health, said that one year previously he had first noticed the appearance of raised, annular lesions on the forearm, one-half inch or more in diameter. About six months later, similar lesions appeared on the lower portion of the legs, the largest being about the ankle. The lesions were annular in arrangement, and the area in the center of the patches was somewhat depressed. They first appeared as small nodules, firm and pinkish to violaceous, gradually attaining the size of a pea, and forming in groups. There had been no subjective symptoms.

DISCUSSION

DR. PERKINS: The appearance of the lesions is suggestive of erythema perstans or urticaria. The configuration suggests syphilis.

DR. WANDER: A diagnosis of granuloma annulare must be considered, but the nodules are unusually numerous.

DR. VALADE: We must think of the possibility of xanthoma tuberosum multiplex, for some of the lesions on the forearm are quite yellow.

DR. BEHN: The configuration of the lesions on the forearm is suggestive of syphilis, but the possibility of xanthoma must be considered also. There are too many lesions for granuloma annulare.

DR. VARNEY: A biopsy examination would be necessary to settle the question of diagnosis in this case. The color seen in syphilitic eruptions is lacking here. The possibility of a tuberculid can be excluded, and it is apparently not granuloma annulare.

DR. JAMIESON: This is almost similar to a case of granuloma annulare which I have seen recently.

DR. WOLLENBERG: I agree with a diagnosis of granuloma annulare.

DR. WILE: This might be an acute form of xanthoma diabeticorum. That possibility could easily be verified or excluded by a determination of blood cholesterin and sugar.

H. J. PARKHURST, M.D., Reporter.

Book Reviews

PROCEEDINGS OF THE INTERNATIONAL CONFERENCE ON HEALTH PROBLEMS IN TROPICAL AMERICA, Held at Kingston, Jamaica, July 22, to August 1, 1924, by invitation of the Medical Department United Fruit Company.

This conference was held on the initiative and through the hospitality of the United Fruit Company. It included among its members many of the foremost men in tropical medicine. This volume of the proceedings of the conference is, therefore, of exceptional interest, and its publication is but another evidence of the progressiveness and intelligence of the United Fruit Company. Fungus infections of the skin, which are of great importance everywhere, show their greatest luxuriousness in the tropics, and it is a matter of especial interest to dermatologists that there are many papers on mycotic infections of the skin included in the volume. Some of these are: Some Observations on Granuloma Inguinale and Cultural Studies of the Donovan Bodies, Foster M. Johns, M.D.; The Treatment of Oriental Sore by Means of Phosphorus, Aldo Castellani, M.D.; Tropical Dermatology, Aldo Castellani, M.D.; Mycosis of the Hands and Feet, C. S. Butler, M.D., J. E. Houghton, M.D., and G. F. Cooper, M.D.; "Pinta" or "Carate," With Special Reference to Treatment, Eduardo Urueta, M.D.; A Review of Ainhum, With Radiographic Demonstration of Its Bone Pathology, A. A. Facio, M.D.; Treatment of Leprosy, Leonard Rogers, F.R.C.P.; Note of the Use of Bismuth Salt in Substitution for Organic Arsenical Preparations in the Treatment of Yaws (Framboesia Tropica), with Special Reference to the Financing of an Anti-Yaws Campaign, A. R. Patterson, M.B.; Notes on the Incidence of Plague in Kenya in Relation to a Recent Migration of Rodents, and on an Experiment in Eradication Carried Out by a Native Tribe, A. R. Patterson, M.B.

These papers, as the volume in general, are well illustrated, and they constitute a useful contribution to dermatology.

The United Fruit Company is unique in the way in which it has handled its medical problems. It has not only seen to it that provisions are made for the care of its employees, but it has done much to foster scientific work in its hospitals and by its medical men. No better illustration can be found of intelligent work in medicine than is being done by its medical department under the direction of Dr. Deeks, who is undoubtedly a forceful man dealing with a wise board of directors. Both are to be congratulated on the outstanding success of the conference.

BEITRAGE ZUR GESCHICHTE DER SYPHILIS INSBESONDERE UEBER IHREN UBSPRUNG UND IHRE PATHOLOGIE IN OSTASIEN. VON DR. KEISO DOHI. Verlag Von Nankodo, Tokyo, 1923. Large octavo volume. Pp. 145, with numerous halftone plates and tables.

In a letter which accompanies this volume, Dr. Dohi, who is professor of dermatology in Tokyo, says that for several years he has been engaged in making an historical study of the progress of medical science in the Orient, especially in Japan and China, and that he will continue this as his life work. It is an historically worth while undertaking, and the results of the work of so eminent a man should prove of great interest. The volume under consideration is a part of the undertaking. It promises well for the other studies.

The first part concerns the historical study of syphilis. We hear so much about the origin of everything in China long before its discovery elsewhere that it is interesting to find that Dohi agrees with the Columbian origin of syphilis, and traces its introduction into China and Japan and the far East from the voyages of Vasco da Gama and the Portuguese discoverers at the beginning of the sixteenth century. The second part of the book concerns the development of the pathology of syphilis, and here he gives an interesting account of the theories and knowledge of syphilis in the far East from the time of the Ming dynasty. It is a revelation to western students to find that there is a considerable early Chinese and Japanese literature on syphilis. The second chapter of the development of the pathology of syphilis is devoted to its evolution in Europe.

The work is concluded by a complete bibliography, a chronologic table of east Asiatic literature on syphilis, a similar table of the European literature and, finally, a complete subject and author index.

This volume is the kind that results from scholarship and devoted enthusiasm. It is a welcome addition to the literature on syphilis.

JAHRESBERICHT ÜBER HAUT-UND GESCHLECHTS-KRANKHEITEN, ZUGLEICH BIBLIOGRAPHISCHES JAHRESREGISTER DES ZENTRALBLATTES FÜR HAUT-UND GESCHLECHTSKRANKHEITEN SOWIE DEREN GRENZGEBIETE. Volume 3. Price, 58 gold marks. Berlin: Julius Springer, 1925.

It is necessary only to call attention to the third volume of this bibliography of dermatology, syphilology, venereal diseases and borderline subjects. Apparently it is a complete bibliography of these subjects, including not only all of the literature but also reports of cases. Its comprehensive index makes it perhaps the most convenient means we have of obtaining the bibliography of any subject in dermatology or venereal disease for the period that the volume covers. It is invaluable to any one who wishes to examine the literature on any dermatologic subject.

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